

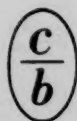
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1941-1942

A. M. BUTLEROV - AN OUTSTANDING RUSSIAN CHEMIST

Academician A. E. Arbuzov

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One hundred years ago on September 19, 1861 (old calendar) in Speyer, Germany, a young professor of chemistry of Kazan' University gave a lecture entitled "The chemical structure of substances" at a congress of naturalists and doctors. The lecture was an outstanding event in the development of theoretical concepts of organic chemistry and marked the beginning of a new stage in chemical sciences.

The theory of the chemical structure of organic compounds, whose basic principles were first put forward by A. M. Butlerov at the congress of naturalists and doctors, gave a powerful impetus to the development of organic synthesis and consequently, the development of the organic chemical industry.

It is difficult to find any other theory in the history of the development of chemistry which has had such a long and outstanding success. Based on a few simple concepts such as the valence of elements and the capacity of carbon atoms to combine to form long threadlike or fantastically branched chains, the Butlerov theory of chemical structure has covered the whole multiplicity of organic compounds for the last hundred years and now extends to other elements in the Periodic Table. The whole of contemporary organic chemistry with more than a million compounds synthesized rests on the Butlerov theory of chemical structure. Only 26 years before the establishment of the theory of chemical structure, the outstanding German chemist F. Wöhler wrote to his famous Swedish teacher, the chemist J. Berzelius: "Right now organic chemistry can drive a person insane. It reminds me of a primeval forest, full of interesting things, monstrous and boundless thickets from which one cannot escape and into which it is frightening to step." A few chemists dared to enter this jungle of organic compounds, but none of them could organize all the tremendous accumulation of experimental material on organic chemistry into an orderly system.

At the beginning of the last century, chemistry was dominated by the electrochemical theory of Davy and Berzelius. According to Berzelius, each chemical compound could be regarded as consisting of two oppositely charged particles and in such typical examples as alkali salts of strong acids, the negatively charged part or acid such as SO_3 (Berzelius considered as an acid what we now call an acid anhydride) was differentiated from the positively charged base such as K_2O . According to Berzelius's electrochemical theory, an acid had to contain oxygen, which he considered as the most electronegative element. However, as early as 1810 Davy could not detect oxygen in the composition of halides, though halogens form true salts with strong bases.

The Berzelius electrochemical theory was considerably undermined by the work of the French chemist J. B. Dumas, who showed in 1834 that in some organic compounds, for example, organic acids such as acetic acid, one, two, or even three equivalents of electropositive hydrogen may be replaced by one, two, or three equivalents of electronegative chlorine without a considerable change in the character of the compound. This reaction discovered by Dumas was called metalepsy. At the same time, this reaction was used by Dumas as the starting point for establishing the so-called theory of types. It should be noted that the French chemist Laurent challenged Dumas' priority to the discovery of metalepsy.

It is appropriate to mention here the difficulty with which new facts and new views were accepted in science and with what stubbornness the supporters of old concepts, in this case the famous Swedish chemist Berzelius, insisted on their scientific theories and convictions. Contrary to the evidence, for a long time Berzelius resolutely denied the similarity in type of acetic and trichloroacetic acids and maintained that the physical properties of these compounds had nothing in common. Dumas wrote in a reply to this objection, which Berzelius considered fundamental: "I have long known that the replacement of hydrogen in a volatile compound by chlorine makes the substance denser and less volatile and increases the density of its vapor; therefore, it is clear that Berzelius's objection does concern the opinion I have put forward." Later in his article, Dumas wrote: "On treating trichloroacetic acid with any alkali, I observed a very interesting reaction: the acid decomposed into two parts—carbonic acid, which combined with the alkali, and free chloroform $\text{C}_2\text{H}_5\text{Cl}$ and furthermore, I was convinced and even predicted in my diary

that acetic acid would be capable of a similar conversion, i.e., that under the action of an alkali it would be converted into carbonic acid (i.e., a carbonate - A.) and a hydrocarbon with the formula C_4H_8 (in present day parlance, CH_4 or methane, -A.). Dumas also noted: "That means that acetic and trichloroacetic acids have the same properties and are of the same organic type."

In extending the concept of replacement or metalepsy, Dumas assumed that the hydrogen in organic compounds may be replaced not only by chlorine or other elements, but also complex groups of atoms or, in other words, radicals, which, according to Dumas, play the part of elements in these cases. Later Dumas came to even broader conclusions. He wrote: "Up to now I have argued as if the law of replacement can be applied only to the replacement of hydrogen, which was observed first, but we should note that carbon . . . and consequently all the elements in an organic compound may be displaced successively and replaced by others."

We should note here that this hyperbolic generalization and enthusiasm of Dumas was subjected at that time to cruel and humorous criticism (I have in mind here the well-known letter by Wöhler), but the very fact of replacement of some elements by others served as a new starting point in the development of theoretical concepts in chemistry.

The next development in theoretical concepts of chemistry, mainly organic chemistry, is due to the French chemists Gerhardt and Laurent. In 1841 Gerhardt was appointed to the chair of chemistry in Montpellier and in preparing a course in organic chemistry for the students, he had to face all the difficulties which inevitably faced each science teacher at that period in the development of organic chemistry when, as a result of the rapid expansion of synthetic chemistry and the existence of a multiplicity of new substances and new facts, the accumulated scientific material could not be covered by the Berzelius electrochemical theory, which still predominated.

The main problems and aims of a research chemist were described by Gerhardt in the following words: "Chemistry is the study of changes in matter; its attention is centered on conversions and this is its main character; it investigates the origin of substances; it notes their past and points out their future; it observes a substance through its various phases until the substance reverts to the initial state. I do not say its end," stated Gerhardt, "because it has no end. Matter is indestructible and only changes its form."

Gerhardt and Laurent's main contribution to the development of theoretical chemistry was the definition of the concepts of atom, molecule, and equivalent weight. Before Gerhardt, chemists quite arbitrarily assigned different atomic weights to various elements (for example, some chemists considered the atomic weight of oxygen as 8 and others as 16, the atomic weight of carbon was taken as 6 and 12, etc.) and this naturally affected the formulas given for compounds.

Gerhardt shared the achievement of defining these fundamental concepts in chemistry with his friend and supporter Laurent. Laurent initiated the important idea that in accordance with the Avogadro-Ampere hypothesis, the volume occupied by a definite amount of substance in the gas or vapor state should be considered as a unit of comparison. We should add here that this proposal by Laurent and Gerhardt at first did not meet with approval from the majority of chemists. One of the reasons for this was the fact that the atomic weights of some elements, for example, the alkali metals sodium and potassium and also silver had been determined incorrectly because of the low standard of techniques and experimental difficulties and this circumstance made many chemists doubt the advantages and value of the reform proposed by Gerhardt and Laurent.

Somewhat later, S. Cannizzaro, the Italian chemist, overcame the difficulties mentioned above. In September 1860, after Cannizzaro's report, the International Congress of Chemists at Karlsruhe adopted a resolution which put forward the principles for defining the concepts of atom, molecule and equivalent. Almost simultaneously, the successive application of the concept of atom and molecule led Gerhardt to the formulation of the so-called unitary system, according to which the molecule of a substance was considered as a single unit. As a result, the unitary system or theory made it impossible to apply the dualistic Berzelius formulas to such compounds as nitric acid, sulfuric acid, caustic alkali, and many others.

In addition, there was one other chemical phenomenon which played an important part in preparing the ground for the formulation of the theory of chemical structure and this was isomerism. At the beginning of the nineteenth century, even such great intellects as Berzelius considered that the properties of chemical compounds were determined wholly by composition. Therefore, when in 1824 J. Liebig and F. Wöhler established the composition of silver fulminate and consequently the composition of fulminic acid itself and then Wöhler showed by analysis that cyanic acid had exactly the same composition as fulminic acid, all these new facts attracted the greatest attention from

chemists. It seemed most surprising to chemists of that time that these acids as well as their salts had completely different properties. As regards these phenomena, which were quite incomprehensible to him, Berzelius first declared that they were the result of incorrect analyses, but, we should add, the analyses were carried out by such brilliant and experienced experimenters as Liebig and Wöhler.

Facts similar to the above soon became more numerous and finally Berzelius himself was convinced that racemic and tartaric acids and also their salts had different properties, although their compositions were the same. Berzelius then recognized the existence of such facts and named the new phenomenon isomerism (from the Greek words *ισος* equal and *μέρος* part). The phenomenon of isomerism undoubtedly had to lead chemists to the idea that the difference in the properties of two isomeric substances must be due to a difference in their structure.

Attempts to represent a complex chemical body as consisting of simpler parts had been made long before by some chemists. Thus, even before Lavoisier, Guyton de Morveau had put forward the concept of a definite part of an acid, in other words, an acid radical. Later, the concept of a radical was extended by Lavoisier, who considered that a radical could be simple or complex, i.e., consisting of several atoms in the latter case. Berzelius accepted this concept of a radical given by Lavoisier and extended it. We find Berzelius writing that the difference between organic and inorganic bodies is that in the inorganic world, all oxidized bodies contain a simple radical, while organic bodies consist of oxygen compounds of complex radicals. Can radicals or, in other words, parts of a chemical body exist independently? Berzelius did not give a definite answer to this important question.

On the basis of some experimental data, many chemists concluded that radicals can exist independently. Examples are the cyano radical of Gay-Lussac and Bunsen's cacodyl. We should note here that these conclusions were erroneous as it was found that the cyanogen molecule consists of two cyano radicals and Bunsen's cacodyl molecule consists of two cacodyl radicals, etc. Nonetheless, it was established in science that complex bodies could be represented as consisting of simpler parts.

The next step which brought chemists closer to the formulation and then the solution of the problem of the structure of organic compounds was the doctrine of the atomicity or, in other words, valence of elements. Credit for establishing the concept of the atomicity of elements belongs to the British chemist E. Frankland. In 1852 Frankland established that "the affinity (or saturation capacity of the elements forming a compound was always satisfied by the same number of atoms adding to them, regardless of the chemical nature of the atoms." At first, Frankland applied this rule to inorganic and organic compounds which were derivatives of nitrogen, phosphorus, arsenic, antimony, and tin. Later the German chemist Kolbe (1857) extended Frankland's idea to purely carbonaceous compounds and recognized carbon as a tetravalent element, though, at the same time, allowed the possibility of divalent carbon, for example, in carbon dioxide, and even trivalent carbon.

Independently of Kolbe, in 1857 the German chemist Kekule also recognized the tetravalence of carbon and gave the formulas of methane and carbon tetrachloride as the simplest examples. The following year, 1858, A. Kekule made an important advance and extended the concept of the tetravalence of carbon to compounds containing several carbon atoms and thus he came to the conclusion that chainlike attachment of carbon atoms was possible in polycarbon compounds. Later, Kekule came right up to the problem of the structure of carbon compounds, but did not take the decisive step in this direction. Thus, at the end of his article in 1858, Kekule stated: "In conclusion, I consider it necessary to note that I myself assign only secondary importance to discussions of this type" (i.e., discussions on structure. — A).

We should add that Kekule remained under the influence of Gerhardt's ideas for a long time and in his well-known textbook on organic chemistry, which was published in 1859-1861, he made extensive use of "rational" formulas in the same way as Gerhardt. The following examples confirm what has been said: Kekule gave four formulas for acetaldehyde and four also for acetone, etc. Only as an exception, Kekule gave several extremely unwieldy structural formulas based on the valence of elements.

Almost at the same time as Kekule's article, an article entitled "A new chemical theory" was published in three languages by the young British chemist A. Couper. Independently of Kekule, Couper concluded that it was necessary to start from the concept of the valence of elements to gain an insight into the structure of compounds and their possible conversions. In his article, Couper gave a series of structural formulas as examples and these resemble in many ways modern structural formulas of organic compounds. In addition to these, there were also incorrect formulas such as those for oxalic acid, glycerol, etc. included in Couper's article.

A. M. Butlerov, who had been following attentively the flow of scientific ideas in the West, considered it necessary to criticize the new theory of A. Couper. Couper's scientific activity ended suddenly and he did not have time to publish the second article he promised on the structure of organic compounds. Quite a while after Couper's article, an article was published by the German physicist I. Loschmidt in which a huge number of "constitutional formulas of organic chemistry represented graphically," as Loschmidt put it himself, were given in the basis of purely theoretical considerations. There are quite a few incorrect formulas, for example, that of benzoin, given among the ingeniously expressed formulas. I would like to stress here that the purely speculative attempts by Couper and Loschmidt to represent the structure of organic compounds, which were not based on the tremendous accumulation of material in synthetic chemistry nor founded on any new data, were hardly considered and therefore had no effect and could not have had any effect on the development of the problem of the structure of organic compounds.

Such is the rough picture of the state of theoretical ideas in chemistry, largely of carbonaceous compounds, up to the end of the fifties of the last century. Briefly summarizing, we can say that the attempts of outstanding Western chemists, among whom we should first mention Kekule, Kolbe, and Couper, to find new basic concepts for the further development of the chemistry of organic compounds gave no tangible results. As previously, both the teaching of organic chemistry and research work were based on the Gerhardt system.

However, it was felt that a new epoch in the development of chemistry was approaching, but the genius Butlerov was needed to cross the Rubicon and push science forward. However, we should not imagine that it was easy for Butlerov to cross the Rubicon. Butlerov himself in 1858, after returning from his first trip abroad, read a course in organic chemistry to his students based on Gerhardt's system, but at the end of 1858, Butlerov wrote in an article entitled "Comments on the new chemical theory of Couper" that "the time has come to go further than Gerhardt."

In a course of lectures he gave to his students in 1860, Butlerov started to put forward carefully the basic principles of his theory of chemical structure. The ideas of Gerhardt moved to second place. This was the time of the full flowering of Butlerov's creative talent; in a short period, the young professor of a provincial university developed into an outstanding, progressive scientist, who, in contrast to most Western European scientists, defined with unusual clarity and fullness the successive problems of theoretical chemistry and the possible ways of solving them.

Butlerov's theoretical ideas took on a finished form and he decided that he should introduce his new ideas and opinions to Western European scientists. With difficulty, Butlerov obtained permission for a second trip abroad and in 1861 he again visited all the most important scientific centers in Europe. During his first trip abroad, Butlerov wins our admiration with the incredible rapidity with which he, up to then a young, unknown scientist, learns all the currents, details, and nuances of Western European chemical thought, while his second trip abroad is even more astonishing. According to Butlerov himself, during the first trip abroad he came to "learn," while in his second trip, he could already "teach." During his first visit to Western Europe, Butlerov became acquainted with the general state of chemical science as well as the opinions and points of view of individual scientists, while during his second stay abroad, he found it necessary to put forward to foreign scientists the basic premises of his own chemical ideas and the concrete conclusions he had drawn. Such an occasion presented itself to Butlerov at the 36th Congress of German Naturalists and Doctors in Speyer.

At this congress, in the presence of many outstanding scientists, Butlerov read his well-known report "Einiges über die Chemische Struktur der Körper," the translation of which is "A contribution on the chemical structure of bodies." This short, historical report showed Butlerov's outstanding talent as a theoretician, illustrated by the definition of an important chemical problem and the method of solving it. Later, in 1862, this report with a few editorial additions was published in the "Scientific Reports of Kazan' University" under the title "The chemical structure of matter." This historical report began thus: "Now, after the discovery of many unexpected and important facts, almost everyone recognizes that the theoretical side of chemistry lags behind its factual development and the theory of types, which is accepted by the majority, is inadequate." Then later in his report, Butlerov stated the basic premises of his theory of the structure of organic compounds.

First of all, this includes a definition of the concept of "chemical structure," which Butlerov formulated as follows: "Starting with the idea that each chemical atom in a substance participates in the formation of the latter and contributes to it a definite amount of its inherent chemical force (affinity), I consider that chemical structure is the distribution of the action of this force and as a result the chemical atoms, affecting each other directly or indirectly, combine into a chemical particle." This definition of Butlerov's is so profound and inclusive that it agrees basically with what we at present consider to be chemical structure in the light of the newest chemical concepts on the structure of chemical particles (molecules).

Also very important, particularly for that time, was the part of the report where Butlerov talked of the possibility of determining the structure of a molecule by chemical methods, in particular, by the synthesis of organic compounds. On this cardinal problem Butlerov stated in his report: "Most probably the chemical structure of substances may be deduced best from a study of the means by which they are formed synthetically and, predominantly, by syntheses carried out at low temperatures and, generally, under conditions where it is possible to follow the course of the gradual elaboration of a chemical particle." However, the most vital section in the report is that on the problem of expressing the structure of substances by formulas.

Butlerov's opinion on this fundamental problem differed sharply from the views and convictions of all his predecessors; in contrast to Gerhardt, Kekule, Kolbe and other chemists, Butlerov considered that it was possible and necessary to express the structure of a definite compound by only one formula. This part of Butlerov's report is the place where I consider Butlerov crossed the Rubicon; it is this which gives us the right to claim Butlerov as the true founder of the theory of chemical structure.

The reception given by the majority of the chemists present at the Speyer conference to this first major contribution by Butlerov is most interesting and indicative; briefly, the audience gave it a cold reception. One of Butlerov's most outstanding pupils, V. V. Markovnikov, wrote later on this subject that "Of all the chemists of that time, only the old man Heinz and the young lecturer Erlenmeyer accepted completely the new viewpoints and started applying them in their articles; Wislicenus soon joined them."

This situation was most indicative of the uncoordinated state of mind of Western European chemists on the most basic problems of theoretical chemistry.

Quite noteworthy is Butlerov's own opinion on the results of his second trip abroad expressed in his report to the Board of Kazan' University. Butlerov's acute observations on the dominant scientific trends in the field of chemistry as well as on the individual opinions of prominent Western European chemists is an outstanding feature of this report. The report shows Butlerov's firm stand regarding the dominant scientific trends and this shows that he was more than the formulator of a new and most progressive trend in chemical thought. Butlerov regarded the development of science as a historical process. From this he derived his idea on the role of theories in this process. Fundamentally, Butlerov's viewpoint is based on the idea that a theory must arise from facts, which it is called upon to explain and the theory remains accurate within the limits of these facts.

In time, new facts appear which cannot be or are difficult to explain by an existing theory and the theory must then give way to new and wider generalizations. On this subject Butlerov wrote, "A new outlook is usually wider than the preceding ones; it is preferable as it examines facts from a new aspect and indicates analogies which had remained unnoticed, but this does not make old opinions incorrect as long as they remain within the limits of the facts pertinent to them." It was this latitude and thoroughness of Butlerov's scientific ideas, combined simultaneously with caution and well-based scientific conclusions and deductions which raised the Kazan' chemical laboratory, directed by Butlerov, to the position of an outstanding scientific center.

On his return from abroad, Butlerov developed his scientific work so that it expanded simultaneously and harmoniously in two directions: theoretical and experimental.

First of all, Butlerov wrote a series of articles in Russian and German in which he developed in greater detail his new doctrine on the structure of organic compounds. In these articles Butlerov showed very convincingly a series of errors and inconsistencies found in the scientific arguments of some of the most prominent Western European theoretical chemists, such as Kekule, Kolbe, and Erlenmeyer.

Not satisfied with the development of new theoretical concepts, Butlerov concluded that for the recognition and consolidation of his new doctrine, new facts were needed which followed from this doctrine and he undertook extensive research. The main result of this period of his experimental investigations was firstly, the famous Butlerov synthesis of trimethylcarbinol, which was the first example of tertiary alcohols, whose existence and structure were predicted on the basis of his theory. We should note here that in this work Butlerov again showed himself a skillful experimenter. The synthesis of trimethylcarbinol, starting with phosgene and methylzinc, is extremely complicated. It suffices to say that the Austrian chemists Pebal and Freind could not sort out this reaction and Butlerov was able to achieve this synthesis and isolate trimethylcarbinol only after much work.

Butlerov rapidly appraised the whole significance of this synthesis and guided by his theory of chemical structure, he prepared without much trouble a series of trimethylcarbinol homologs based on various acid chlorides and

organozinc compounds. By these historical syntheses, Butlerov was the first to establish, in agreement with his theory, cases of isomerism among tertiary alcohols. In particular, he found that methyldiethylcarbinol was isomeric with dimethylpropylcarbinol. From the time when Butlerov synthesized the tertiary alcohols, his theory of chemical structure began to triumph.

At the same time as Butlerov achieved his historical syntheses, the opinions of many Western European chemists regarding the theory of chemical structure changed and the number of adherents to Butlerov's theory grew rapidly. Simultaneously, articles appeared in Western European chemical literature by authors who contested Butlerov's priority in formulating the theory of chemical structure. Although few, the baseless pretensions of Western chemists gave Butlerov many unpleasant moments.

During this period of Butlerov's greatest creativeness he made another important contribution, namely, he undertook the publication of his famous textbook, or rather guide, "Introduction to the Complete Study of Organic Chemistry," which first appeared in 1864 in Russian and the whole publication was completed in 1866. The appearance of Butlerov's "Introduction" had a great effect in disseminating his new doctrine among chemists.

Butlerov then made a further and equally important contribution in this direction by deciding to publish his "Introduction" in German. The German translation written by the teacher of German, Reshem, in Kazan', was edited by Butlerov himself and published in Leipzig in 1868. The publication by Butlerov in Russian and German of his textbook on organic chemistry in which the theory of chemical structure was for the first time successively applied to all classes of organic compounds known at that time as well as his brilliant syntheses helped to win wide recognition and consolidate his theory among the chemists of the whole world. The publication of "Introduction to the Complete Study of Organic Chemistry" marks the end of Butlerov's scientific activities in Kazan'. The intense mental strain of publishing the "Introduction" and extensive research had tired Butlerov and both for health reasons and for editing the German translation of his "Introduction," he decided to go abroad for the third time.

Butlerov remained abroad for about a year. While abroad, Butlerov again had the opportunity to meet many prominent chemists and in his discussions with his foreign colleagues he spoke of his point of view and of the future development of the theory of the chemical structure of organic compounds. In the spring of 1868 when Butlerov was still abroad, at the suggestion of D. I. Mendeleev, the Board of professors of St. Petersburg University elected him to an ordinary professorship in the department of chemistry, a position vacated by the retirement of Professor A. A. Voskresenskii. In his nomination, D. I. Mendeleev described Butlerov as a scientist in the following glowing terms: "Aleksandr Mikhailovich Butlerov . . . is a remarkable Russian scientist. He is Russian both in scientific education and in the originality of his work. A student of our famous Academician Zinin, he became a chemist not abroad, but in Kazan' and it is there that he continues to develop his independent school of chemistry. The trend of Butlerov's scientific work belongs to him and is not the continuation or development of the ideas of his predecessors. There exists in chemistry a Butlerov school and a Butlerov trend (my italics - A).

A. M. Butlerov accepted the tempting offer of the Board of St. Petersburg University and sent his acceptance of the chair of chemistry from abroad. Butlerov was confirmed as an ordinary professor of St. Petersburg University in September, 1868. When he returned from abroad, at the request of the Board of the Kazan' University, Butlerov remained in Kazan' till the end of the semester to finish the course.

On February 22, 1869 the Board of Professors of Kazan' University elected Butlerov an honorary member in recognition of his scientific services. An oil portrait of Butlerov was hung in the professors' reading room in the university. At present this portrait is in the assembly hall of the university.

At the beginning of 1869 Butlerov moved to St. Petersburg and on January 23, read his first lecture. In March 1870 A. M. Butlerov was elected Assistant of the Academy of Sciences, in the following year, Extraordinary Academician and in 1874, after the death of Academician Fritzsche, Ordinary Academician.

During his first year in St. Petersburg, besides his teaching duties, Butlerov was occupied with the organization of the laboratory. However, even after the considerable improvements brought about by Butlerov, the laboratory was inferior to that in Kazan'. It is sufficient to point out that twelve persons could hardly work simultaneously in the renovated St. Petersburg laboratory. However, even under these conditions Butlerov with his inherent energy rapidly organized the scientific work; capable young people appeared in the laboratory and it produced numerous papers, which were printed mainly in the new journal of Russian chemists "The Journal of the Russian Chemical Society."

I cannot examine in a short article the numerous papers by Butlerov during the St. Petersburg period. I will only state that all of them consolidated and widened the scope of the theory of chemical structure; like all Butlerov's previous reports, they were outstanding in the profundity of the problems tackled and brilliant experimental resolution.

I should note that all the investigations of the St. Petersburg period were a continuation both in content and trend of the famous work of the Kazan' period. I will clarify this statement further. Thus, on the basis of his synthesis of trimethylcarbinol in 1864, Butlerov developed a series of investigations which had both theoretical and practical value. In his article "Derivatives of trimethylcarbinol," printed in the Scientific Reports of Kazan' University in 1867, on the basis of his theory, Butlerov predicted the existence of two isomeric hydrocarbons with the composition C_4H_{10} , namely, diethyl (butane) and trimethylformene (isobutane). I should note that outstanding chemists such as K. Schorlemmer and A. Wurtz were skeptical of such predictions by Butlerov. By a series of irreproachably organized investigations, Butlerov brilliantly confirmed his theoretical deductions on the existence of the two isomers, butane and isobutane. In the same article Butlerov described the preparation of an unsaturated hydrocarbon C_4H_8 with a branched chain, namely, isobutylene, which, as could be expected, was found to be an isomer of the known hydrocarbon obtained by de Luine.

In these complicated investigations, Butlerov also observed the partial polymerization of unsaturated hydrocarbons. If we also mention that Butlerov included not only such hydrocarbons as isobutylene in his investigations, but later such simple hydrocarbons as ethylene and propylene (although experiments with the last two were unsuccessful for reasons that we can now understand), then it becomes quite evident that Butlerov's investigations, begun in Kazan', are the starting point of the polymerization processes which are of great theoretical and practical interest at present.

It is remarkable that Butlerov who, it seemed, was completely absorbed by the problem of consolidating the theory of chemical structure, still took every opportunity to study the preparation of compounds by methods that were suitable for large scale production. This includes, for example, his experiments on the conversion of ethylene to ethanol and the preparation of isobutane and isobutylene by convenient means. Now the preparation of the hydrocarbons and alcohols which Butlerov studied has reached a colossal scale and their industrial production is measured in hundred-thousands and millions of tons.

It is doubtful whether every technologist, or even maybe chemist, recognizes the importance of Butlerov's work in the development of industry. Thus, synthetic butadiene or Lebedev rubber is still partly prepared from ethanol; the so-called butyl rubber is prepared from isobutylene. Synthetic ethanol and isopropanol are used in great quantities as solvents. The requirements of modern technical industry for hydrocarbons containing quaternary carbon atoms, the 100 octane fuels needed for running airplane engines, are huge and may be said to be limitless.

1880 was the thirtieth year of Butlerov's work. Tired by his intense scientific and teaching activities, Butlerov informed the University Board in October 1879 of his decision to leave the university and on April 4, 1880 he gave his last lecture to the students. His laboratory assistants and students, concerned at the unexpected departure of their teacher, presented him with a collective petition in which they asked Butlerov to reconsider his decision. Butlerov acceded to the request of his colleagues and students and remained for a further five years in the university.

In the spring of 1885 Butlerov finally stopped teaching, but continued his research in the laboratory of the Academy of Sciences. One of Butlerov's closest students, Academician V. E. Tishchenko wrote the following on Butlerov's research and activities in the Academy: "As he carried them (his duties - A.) out with his inherent seriousness and conscientiousness, he had to take up a stand which was the source of much unpleasantness to him. Like Lomonosov, he had to struggle against the majority then ruling the Academy. Butlerov could not but note that in filling vacancies in the membership of the Academy and in awarding prizes for scientific work, there was a tendency to favor foreigners, even when there were worthier Russian scientists. Arousing much opposition, he defended the statute of the Academy which required that, with all other conditions equal, preference should be given to Russian scientists. A struggle ensued, which was particularly aggravated by the vote against D. I. Mendeleev.

After the death of N. N. Zinin (1880), A. M. Butlerov together with Academicians P. L. Chebyshev, F. V. Ovsyannikov, and N. I. Koksharov proposed to the 1st Division of the Academy of Sciences the nomination of D. I. Mendeleev for active membership of the Academy of Sciences. Butlerov concluded his representation with the following words: "Professor Mendeleev takes precedence in Russian chemistry and sharing the general opinion of Russian chemists, we consider that it is his right to have a place in the leading scientific body of the Russian empire. By including Professor Mendeleev, the Academy would be honoring Russian science and itself, as its highest represen-

tative." However, as is known, D. I. Mendeleev, whom N. N. Beketov called "Russia's scientific pride," was outvoted for the second time. Deeply indignant at such cruel injustice, Butlerov was not afraid to come out openly in print with his famous article: "Is the Academy of Sciences in St. Petersburg Russian or only imperial?" This struggle with the reactionary majority of the Academy adversely affected Butlerov's health.

During the last period of his academic activity, Butlerov reduced his laboratory investigations and turned more and more to the consideration of difficult problems of theoretical chemistry of long range value. These speculations of Butlerov illustrate again his genius and exceptional intuition in predicting the future stages of chemical science. One can say that Butlerov guessed and not only guessed, but plotted the course of his well loved science for many decades ahead. This particular feature of Butlerov's mind is kindred to Lomonosov's genius.

I will give a few examples to illustrate the above. Thus, in the article "Various explanations of some cases of isomerism," Butlerov wrote: "I do not believe that it is impossible, as Kekule considers, to represent on a plane the position of atoms in space." There is no doubt that this excerpt expresses Butlerov's thoughts on the development of the theory of chemical structure into stereochemistry.

Butlerov expressed some very valuable thoughts on the nature of chemical phenomena which were later called "tautomerism" (reversible isomerism). Thus, as early as 1862, on the example of cyanic and isocyanic acids, Butlerov stated that there may be cases where a definite substance reacts as if it has two structural forms. Later, in an article "Diisobutylene, one of the modifications of octylene" (1877), Butlerov returned to this problem and interpreted remarkably well cases of reciprocal isomeric conversions of one structural form of a definite substance into another. The German chemist Laar, who gave the name tautomerism to cases of similar conversions, first claimed the honor of having discovered this new chemical phenomenon and gave it an unsubstantiated explanation, which assumed the possibility of so-to-speak two structures at the same time, but after a letter from Butlerov, he admitted the accurate interpretation and priority of the Russian scientist. Later, in studying the many cases of tautomerism that were discovered, chemists using chemical and physical methods confirmed fully the explanation given by Butlerov for these peculiar chemical conversions.

I must mention at least briefly that in these years of his most intense scientific activity, Butlerov spread his ideas widely as is illustrated by the special course of lectures he gave in 1879-1880. This course was called "A historical outline of the development of chemistry in the last 40 years." It is most characteristic of Butlerov's wide scientific outlook that he wrote on the title page of the typed course of lectures a quote from the famous English philosopher F. Bacon: "Truth is the daughter of time and not of authority." In this course of lectures, in historical sequence and with great objectivity, Butlerov unfolded before his listeners the complex and often contradictory picture of the development of facts and ideas which finally resulted in his theory of chemical structure. Butlerov finished his historical sketch with the following words, addressed to the young generation: "Let us hope that in glancing at the past, young chemists will learn from it to work for greater good in the future."

While consolidating his theory of chemical structure, Butlerov continued to evolve his ideas on fundamental and most important and difficult problems of theoretical chemistry. His thoughts and statements on the constancy of atoms and atomic weights of elements were as follows. Butlerov considered that Prout's hypothesis was actually true; however, at the same time he assumed that there may be small deviations in the atomic weights of elements. Thus, in his pamphlet "Fundamental concepts of chemistry" Butlerov wrote: "At the beginning of this outline it was stated that elements are substances which have not yet been decomposed, but the chemical complexity of some of them (even though of a particular type) is not improbable. This means that the "atoms" of some elements, as they are considered now, may actually be capable of chemical decomposition, i.e., they are not indivisible by nature, but only indivisible by the means available to us and remain so only in those chemical processes which are known at present and may be decomposed in new processes which will be discovered in the future." Butlerov thus concludes his thoughts: "Such a strict interpretation of the concept of an atom corresponds fully to the spirit and actual meaning of scientific theories."

In evolving his thought on the possible division of atoms, which was so brilliantly confirmed in our time, Butlerov progressed further and put forward a question that was just as important, namely, that of the constancy of the atomic weight of elements. Regarding this question, Butlerov wrote in his "Note on atomic weights"; "I pose the question: will not Prout's hypothesis be completely accurate under certain conditions (which we are not yet in a position to define)?" Butlerov continues: "To pose such a question means a decision to deny the absolute constancy of atomic weights and I actually think that there is no reason to accept this constancy."

Further, Butlerov wrote: "... To chemists, atomic weight will mainly be nothing more than a term expressing a certain amount of matter carrying a known amount of chemical energy. But we know well that the amount of energy is determined not only by the mass of the substance in the case of different forms of energy: the mass may remain the same while the amount of energy changes, nonetheless, for example, as a result of a change in velocity. Why then should there not exist similar changes in chemical energy even within the known strict limits?" These words of Butlerov are prophetic as we can see in them the beginnings of our modern concepts of the relations between matter and energy.

An interesting question for the present time is the attitude of the great scientist A. M. Butlerov toward the relation between science and practice. He gave a lecture on this theme at the grand meeting of the Academy of Sciences on December 29, 1870 under the title "The practical value of scientific chemical work." Butlerov started his lecture as follows: "Science has a free and facile life only when it has the full interest of the society. Science will be able to count on this interest if the society is closely related to it. The society then recognizes that the needs of science are its own and that science is the best source of strength for the society and that the paths of knowledge and development always coincide, regardless of the direction taken."

Butlerov expressed himself very clearly on the value of scientific theories at the end of the lecture: "Only after the understanding of phenomena, the formulation of generalizations and theories, and the comprehension of the laws governing the phenomena is there a beginning of true human understanding and science arises. As with all other organisms, man, being completely dependent on the effects of nature, is also subject to the general law of the survival of the fittest. Lacking most of the natural defenses which are inherent in beings of a lower order, man possesses instead a stronger weapon in his ability to abstract and generalize. By nature he must use them; he is duty bound to use them in order to remain in his position at the top of the order of organisms. True knowledge gives him a strength that is inaccessible to other beings. It is this knowledge alone which makes it possible to direct the forces of nature according to set aims."

The outstanding role of the great scientist Butlerov in the expansion of science culture would not be fully described if we limited ourselves to the scientific side of his activities.

The period of Butlerov's highest scientific creation coincided with the period of social advance in Russia known historically as the Movement of the Sixties.

Being sensitive and responsive to all that was progressive, Butlerov could not remain isolated from the social advance and social life. Thus, while Butlerov was apparently totally immersed in the solution of complex chemical problems and his laboratory investigations, he spent part of his time in social service. In the fifties in St. Petersburg, a small group of chemists would meet at each others houses in turn to discuss the latest news in chemical science. At the beginning of the sixties, on their own initiative, the chemistry professor N. N. Sokolov and a well-known journalist and public-spirited man, A. N. Engel'gardt, who was interest in problems of chemistry and efficient agriculture, started publishing the "Chemical Journal."

At the suggestion of the well-known zoology professor K. F. Kessler, the first Congress of Russian Naturalists and Doctors met in St. Petersburg in 1868. As a result of this congress, several scientific societies were organized, including the Russian Chemical Society initiated by D. I. Mendeleev and N. A. Menshutkin. N. N. Zinin was the first editor of the society and remained in the position for ten years. In 1869 A. M. Butlerov was elected a member of the society and soon became one of its most active members. In 1878 N. N. Zinin refused to continue as president despite the urgent requests of the society members. A. M. Butlerov was elected president after N. N. Zinin and he remained in the position for three years. In 1883, despite urgent requests, Butlerov refused to be reelected. The society made Butlerov an honorary member and his name was included in the list of members in perpetuity.

Butlerov was an ardent supporter of higher education for women. Thus, 1870 Butlerov participated actively in the organization of higher courses for women. These were named "Bestuzhev" courses in honor of one of the founders, the history professor (later Academician) K. N. Bestuzhev-Ryumin. These courses could have been called "Butlerov," if Butlerov had not modestly refused the honorable title of "founder of the courses." In the spring of 1886, when a well-known reactionary minister of public education, Count Delyanov, had forbidden further courses, Butlerov put forward the idea of establishing universities for women. Butlerov kept repeating, "We should aim for not only higher courses, but also universities for women, including all departments, in each university town."

All that I have reported still does not exhaust the extensive scientific and social activities of Butlerov.

An eminent theoretician and experimenter, Butlerov willingly gave public lectures on subjects which were directly related to practical problems. Examples are his well-known series of lectures, "Water, "Illuminating gas," etc. Butlerov's public lectures always included a demonstration of carefully planned and prepared experiments. Butlerov's extensive scientific and social activities gave him immense authority. Butlerov was the founder and creator of the scientific trend in organic chemistry which has been for a hundred years the inexhaustable source of an infinite number of discoveries of equal theoretical and practical importance.

Butlerov was the founder and head of the famous "Butlerov school of organic chemists," which one can claim extended its effect to not only all the scientific centers of our country, but far beyond its frontiers. Of the representatives of the Butlerov school who were students of Butlerov himself or students of his students, we should, first of all mention V. V. Markovnikov, A. E. Favorskii, V. E. Tishchenko, D. P. Kononov, A. I. Gorbov, N. M. Kizhner, S. V. Lebedev, S. N. Reformatskii, as well as many others. This success of Butlerov's scientific activity is due not only to his high talent as a scientist, but to his very high qualities as a man.

Butlerov was very well characterized by one of his closest students, G. G. Gustavson, who was a co-worker in St. Petersburg University for a long time. Gustavson reminisced, "The lively geniality, sociability, and remarkable delicacy attracted everyone to him. Another strong trait in Butlerov's character, which resulted in the flowering of his school, was his persistence and particular aspiration to complete and exhaust each matter."

Gustavson also emphasizes another aspect. "Butlerov always worked openly, in the sight of all his co-workers. All the finest matters which required particularly intense attention he carried out before the eyes of everyone, often during a lively discussion. I have every reason to state," continues Gustavson, "that he thought openly . . . He had no secrets either in ideas or in attempts to achieve them."

Butlerov's intense activities ended suddenly. In March 1886 Butlerov injured his leg by a careless movement and he was sent to bed by his doctors. The sudden illness was tedious to his lively and active nature, but was not serious. He was soon well and went to Butlerovka for the summer. Butlerov felt well in the village and his leg did not pain him. However, on August 5 Butlerov felt ill and after several hours of suffering, died, quite unexpectedly to all his relatives. Butlerov was buried in the family chapel close to the village of Butlerovka.

It is the debt of Soviet chemists to develop creatively and expand the great scientific heritage of Butlerov, his theory of chemical structure, in the light of the latest discoveries of science.

INVESTIGATION OF CALCIUM PEROXOTUNGSTATES. I

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Catalytic decomposition of hydrogen peroxide under the influence of salts of calcium and tungsten has been studied by G. A. Bogdanov and T. I. Berkengeim [1]. It has been established that the process takes place according to the pattern of a homogeneous catalytic reaction and is dependent on the formation of two intermediate products differing in composition and activity—peroxotungstates of calcium which have not been described in the literature.

In the present work we set up for ourselves the problem of studying the physicochemical properties of the calcium peroxotungstates.

Preparation of Calcium Peroxotungstates

White $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ and yellow $\text{CaWO}_8 \cdot n\text{H}_2\text{O}$ are not very stable compounds; the two products can be isolated only under low-temperature conditions and the preparation of CaWO_8 is carried out with greater cooling.

As the starting material for the preparation of the calcium peroxotungstates we used calcium tungstate CaWO_4 , which was obtained by an exchange reaction between saturated solutions of calcium chloride and sodium tungstate. The CaWO_4 was freed of impurities by repeated washing with twice-distilled water.

Preparation of CaWO_8 . Calcium tungstate was added in small portions with continuous stirring to 55% hydrogen peroxide cooled with dry ice.

To accelerate the reaction and avoid supercooling, the reaction mixture was periodically taken from the dry ice and warmed to -5 to 0° . Above this temperature decomposition of the product takes place rapidly.

For full completion of the reaction the mixture was left in the dry ice for 2-2.5 hours and after this it was filtered, with intense cooling, from the unreacted tungstate. The CaWO_8 was readily soluble in water and was contained in the filtrate (it was also necessary to greatly cool the flask for the filtrate). The CaWO_8 was precipitated from the filtrate by very cold alcohol. Coarse yellow needle-shaped crystals immediately precipitated and were filtered off, also with strong cooling. The material obtained was washed 6-8 times with cold alcohol and was analyzed for peroxide oxygen, calcium, and tungsten. The analyses showed that the CaWO_8 obtained by this method was of satisfactory purity.

Preparation of $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$. The white calcium peroxotungstate $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ was prepared in a manner similar to the CaWO_8 [1], but with less cooling. Analyses of the white product showed that its composition corresponded exactly to the formula $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$.

Experimental Methods

The investigation of the kinetics of decomposition of the calcium peroxotungstates and the electroconductivity of their solutions was carried out simultaneously for the same reaction mixture.

For this purpose we used a flask with sealed-in polished platinum electrodes, since it had been established in advance that smooth platinum, in contrast to platinum black, does not catalyze the decomposition of H_2O_2 ; it also does not affect the decomposition of peroxide compounds (the kinetic curves obtained with polished platinum electrodes and without them are superimposed).

The kinetics of the decomposition was studied volumetrically, and the electroconductivity was recorded during the course of the entire catalytic process after each 2 ml of oxygen that was evolved. The measurements were made with the aid of a type R-38 slide-wire bridge, using an ÉO-6M oscillograph.

The results of the kinetic and electroconductivity measurements are shown graphically.

Investigation of Kinetics of Decomposition of $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ and $\text{CaWO}_5 \cdot n\text{H}_2\text{O}$ and Electroconductivity of Solutions

The experiments were carried out under the following conditions: a) at different temperatures, b) at different acidity and alkalinity of the medium, and c) with different amounts of the materials.

In Fig. 1 the results of measurement of the rate of decomposition of CaWO_6 in neutral medium at different temperatures are shown (the rate of decomposition V is expressed in moles/liter \cdot min of O_2 evolved). The amounts of the product used for this whole series of experiments were about 0.7 g, which corresponds to approximately 0.12 M solutions calculated for free H_2O_2 . In this figure the curves for the measurement of electroconductivity of the solutions at the time of the experiments also are shown.

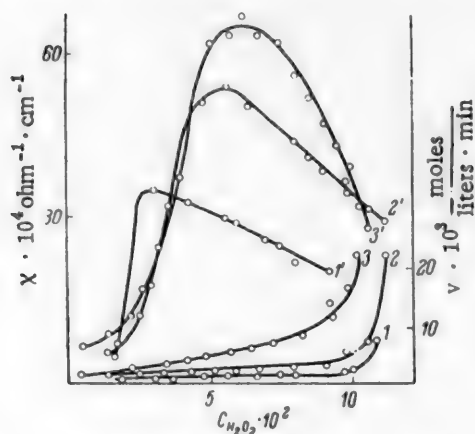
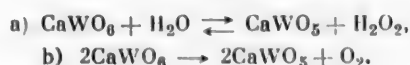


Fig. 1. Change in rate of decomposition of CaWO_6 (Curves 1-3) and electroconductivity of solutions (Curves 1'-3'). 1,1') 25°; 2,2') 35°; 3,3') 45°.

From Fig. 1 it is seen that the kinetic curves have breaks, after which they correspond approximately to a first order equation; the electroconductivity curves pass through a clearly expressed maximum. The change in the rate of decomposition of CaWO_6 when the temperature is increased obeys Vant Hoff's rule.

To characterize the temperature relationship of the rate of decomposition of the white calcium peroxotungstate the values of the temperature coefficients γ and the energy of activation E were found. The average value of the energy of activation for the process of decomposition of CaWO_6 was 26.0 kcal, $\gamma = 4$.

The combination of facts obtained convinced us that in the process of decomposition of CaWO_6 there appears in the solution a new peroxide compound which in all probability is CaWO_5 . This is indicated by the breaks in the kinetic curves. The constant of decomposition of CaWO_5 is less than the constant of decomposition of CaWO_6 . The formation of CaWO_5 in the solution may be accomplished in two ways:



The compound CaWO_5 is readily soluble and has a high electroconductivity, therefore the electroconductivity increases as the CaWO_6 decomposes. The subsequent decrease in electroconductivity is explained by the precipitation of the insoluble salt CaWO_4 which is formed. The study of the kinetics of decomposition and the electroconductivity of CaWO_6 in acid and alkaline media showed that the kinetic curves under any conditions have the characteristic breaks at the beginning of the process. The rate of reaction increases with an increase in pH.

The electroconductivity curves in alkaline medium, as also in neutral medium, pass through a maximum, while in acid medium the electroconductivity has its greatest value at the beginning of the process and then, as the effective concentration of the substrate decreases, it falls, following approximately the rule $\kappa = k \cdot c_{\text{CaWO}_6}$.

It is interesting to note that the electroconductivity in neutral medium is the greatest in absolute value. Addition of acid or alkali to a solution of calcium peroxotungstate does not increase, but on the contrary decreases the electroconductivity of the latter. The hydrogen ions and hydroxyl ions, entering into reaction with the peroxotungstate, form less conductive products and inhibit the genesis of substances having a high electroconductivity.

The H^+ and OH^- ions have a substantial effect on the mutual transition of peroxo and peroxy compounds in solution, which is reflected not only in the absolute values of the electroconductivity, but also in the nature of its change.

Thus when calcium peroxotungstate reacts with the solvent, the following occurs: a) formation of new peroxy structures as a result of peroxo-peroxy form transition b) formation of a new lower peroxide which in all probability is a peroxide containing the radical WO_5^{2-} .

H^+ ions form with peroxotungstate ions relatively stable and only slightly dissociated acid peroxotungstates or weak peroxy acids. OH^- ions inhibit the formation of highly conducting particles in the solution; they may suppress the hydrolysis of the peroxy salt, being themselves consumed in the process.

The curves of Fig. 2 reflect the kinetics of decomposition and the electroconductivity of $CaWO_3$ in neutral aqueous solution at different temperatures. In the figure the results are given for two series of experiments carried out with two different samples of the product. Curves 1-5, which express the relationship of the rate of reaction to the concentration of the substrate, do not have initially those breaks which are so characteristic of $CaWO_6$ (only Curve 6 has a smooth bend characteristic of a 2nd order reaction). This circumstance is associated with the fact that in this case the formation of a lower peroxy compound is hindered.

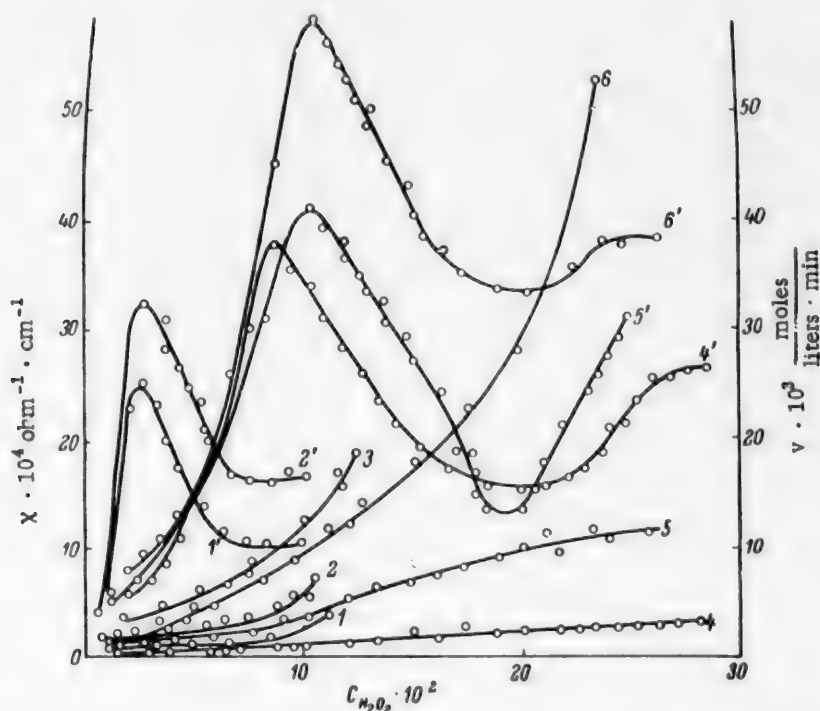


Fig. 2. Kinetics of decomposition of $CaWO_3$ (Curves 1-6) and electroconductivity of solutions (Curves 1'-6'). Sample 0.5 g: 1,1') 25°; 2,2') 35°; 3) 45°. Sample 1.5 g: 4,4') 25°; 5,5') 35°; 6,6') 45°.

The values of E and γ for $CaWO_3$ do not depend on the temperature. But the energy of activation and the temperature coefficient do not maintain strict constancy with a change in the effective concentration of the substrate and increase as the latter decreases. The energy of activation and the temperature coefficient for the decomposition of $CaWO_3$ on the average is $E = 20$ kcal, $\gamma = 3$. It is characteristic that E and γ for $CaWO_3$ have smaller values than for $CaWO_6$.

The kinetic curves 1, 2, and 3 (Fig. 2) obtained with small samples do not coincide with the corresponding curves 4, 5, and 6 for large samples, and at any temperature they are located higher. The disagreement of the curves noted is a result of the stepwise decomposition of $CaWO_3$ in solution and the absence of instantaneous establishment of equilibrium between the calcium peroxotungstate and the solvent.

Curves 1' and 2' for the change in electroconductivity of $CaWO_3$ solutions corresponding to small samples are parallel to the abscissa axis at the beginning of the process, then the electroconductivity increases, passing through a maximum. In contrast to the curves for solutions of $CaWO_6$, the maxima in Curves 1' and 2' of Fig. 2 are located close to the origin of the coordinates. The course of the curves shows that when $CaWO_3$ decomposes, $CaWO_6$ is formed, which then goes over to $CaWO_5$ and finally to $CaWO_4$.

An entirely different picture is given by the curves for the electroconductivity with large samples of CaWO_3 . While the kinetic curves differ almost not at all from the curves for the first series of experiments, the Curves 4', 5', and 6' for the change in electroconductivity of large samples of the peroxo salt are very unique, unlike any known in the literature for peroxy compounds: the curves for the electroconductivity of the solutions pass first through a minimum, then through a maximum.

To clarify the reasons for such a change in the electroconductivity, a series of experiments was carried out on the measurement of the molar electroconductivity of CaWO_3 and CaWO_6 at different dilutions. It proved to be possible

to carry out this series of experiments at low temperature. The data from the investigations carried out permit an explanation of the observed course of the change in electroconductivity of the calcium peroxotungstates in solution.

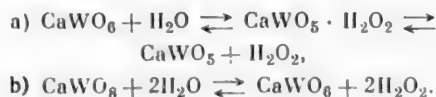
Change in Electroconductivity of Solutions of Calcium Peroxotungstates with Dilution

It can be seen from the above discussion that the stability of the calcium peroxotungstates in aqueous solution depends greatly on the temperature. At room temperature CaWO_3 and CaWO_6 decompose vigorously with the evolution of O_2 . The decomposition of these compounds, however, practically ceases at 0° . In the first minutes of the reaction of the hydrates of CaWO_3 and CaWO_6 with water at 0° an insignificant amount of O_2 is given off, and subsequently the evolution of oxygen is greatly slowed down.

The relative stability of the hydrates of CaWO_3 and CaWO_6 in aqueous solution at 0° permitted investigation of their electroconductivity.

It turned out that the electroconductivity of both CaWO_3 and CaWO_6 changes with time. It is interesting that the electroconductivity of CaWO_6 with respect to the extent that it is present in the solution first increases, then after some time takes on a constant value. In contrast to this, the electroconductivity of CaWO_3 at first decreases, after which it assumes a constant value.

The different change in electroconductivity of the calcium peroxotungstates with time in the absence of their decomposition with evolution of O_2 indicates that these products react with water with the appearance of other products. The following reactions can be assumed:



The products of the hydrolysis reaction (b) have a lower electroconductivity in comparison with (a); the formation of the peroxide CaWO_5 , which has a high electroconductivity, is hindered here under conditions of an excess of H_2O_2 . The establishment of a constant value of the electroconductivity of solutions of CaWO_6 and CaWO_3 corresponds to the attainment of equilibrium with respect to the above equations (a, b).

These data explain the appearance of a minimum and maximum for the electroconductivity in the curves of Fig. 2 and of a maximum in the curves of Fig. 1.

If the assumptions stated are true, then the molar or equivalent electroconductivity in the range of small concentrations of these peroxides should increase sharply with dilution.

The data on the change in molar electroconductivity μ with dilution V are presented in Fig. 3. Dilution of the solutions was carried out both before and after establishment of a constant value of the electroconductivity. In spite of the great dilution, the electroconductivity as a function μ of V increased continuously and did not reach a limit—an asymptotic course was not observed for the curves for solutions of CaWO_6 and CaWO_3 .

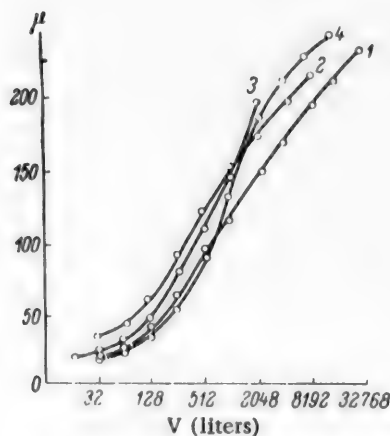


Fig. 3. Change in molar electroconductivity of solutions of calcium peroxotungstates with dilution. 1, 2, 3) CaWO_6 ; 4) CaWO_3 .

One other peculiarity in the behavior of the calcium peroxotungstates consists in the unusually sharp increase in molar electroconductivity with dilution.

For CaWO_6 the ratio $\mu_{1024} : \mu_{32}$ is approximately 5, and for CaWO_8 it somewhat exceeds 5.

If Ostwald's rule is applied formally to our case, then it follows that CaWO_6 and CaWO_8 dissociate into 5 ions.

The absolute values of μ for CaWO_6 and CaWO_8 at $V = 1024$ liters are approximately 110 and 140, indicating that when CaWO_6 and CaWO_8 dissociate two ions are formed.

The data on the electroconductivity leads us to the conclusion that the degree of dissociation for CaWO_6 and CaWO_8 is relatively small, but it increases sharply with dilution. It is essential that in the course of dilution substances are formed which have a high electroconductivity.

This explains the agreement of the data obtained with Werner's rule and their deviation from Ostwald's rule.

One of our assumptions proved to be easy to verify by direct experiments. For this purpose we carried out cryoscopic measurements on solutions of CaWO_6 . We were able to determine the degree of dissociation practically at dilutions of 32 and 48 liters. It actually proved to be small and approximately equal to 0.116 and 0.165, respectively; the dissociation constant for CaWO_6 was about $5.8 \cdot 10^{-4}$.

SUMMARY

1. The calcium peroxotungstates $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ and $\text{CaWO}_8 \cdot n\text{H}_2\text{O}$ have been synthesized in rather pure condition.
2. The kinetics of the decomposition and the electroconductivity of the calcium peroxotungstates have been studied in solution under different conditions. The curves for the decomposition of CaWO_6 have breaks, but the curves for the change in electroconductivity pass through a maximum. The curves for the change in electroconductivity of CaWO_8 are unique: they have contiguous maximum—minimum—maximum.
3. The energy of activation has been calculated for the decomposition reaction of both peroxotungstates.
4. The molar electroconductivity of the peroxotungstates has an anomalous course with dilution. The observed phenomena depend on the consecutive transformation of the peroxide compounds investigated.

LITERATURE CITED

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INVESTIGATION OF CALCIUM PEROXOTUNGSTATES. II

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In the preceding communication [1] methods were described for the synthesis of calcium peroxotungstates and the results were discussed of a study, in solution, of the kinetics of their decomposition and their electroconductivity under different conditions of pH, temperature, and concentration.

The present communication is devoted to an investigation of the dehydration, thermography, and heat effects of decomposition of the calcium peroxotungstates and also to a study of the kinetics of decomposition and the electroconductivity of solutions of the dehydrated peroxotungstates.

Dehydration of Calcium Peroxotungstates

The object of the experiments on dehydration was the elucidation of the nature of the connection of the peroxide groups in the products under investigation. True peroxides usually are dehydrated without loss of oxygen, but peroxyhydrates with a loss of water simultaneously lose the peroxide oxygen.

The reactions proposed by Riesenfeld and Wilstetter for distinguishing peroxo compounds from peroxyhydrates in general are unreliable and do not give well defined results. These reactions do not solve the problem of the relatively mixed peroxides containing peroxooxy groups.

In order to study the dehydration of the calcium peroxotungstates we placed them in a vacuum desiccator on filter paper over P_2O_5 and kept them there for a long time. Samples were taken periodically for analysis of their water and peroxide oxygen contents [2]. The desiccator with the white peroxotungstate over P_2O_5 was at room temperature, and that with the yellow peroxotungstate was placed in the freezing compartment of a refrigerator.

The results of the experiments showed that the white product under these conditions lost water relatively rapidly, while the peroxide oxygen content was unchanged. Upon reaching 3 moles of water per mole of $CaWO_6$ the dehydration sharply slowed down, and at a content of 1 mole of H_2O per mole of $CaWO_6$ the loss of water was retarded still more.

Right up to the formation of the product corresponding to the formula $CaWO_6 \cdot H_2O$ the peroxide oxygen was completely retained in the molecule. Upon further dehydration, however, peroxide oxygen was lost along with the loss of water. It is essential to note that the water was lost more rapidly than the peroxide oxygen. The absence of parallelism in the loss of the number of moles of H_2O and the number of moles of peroxide O_2 and the obvious retardation in the loss of the latter gives us reason to consider that the white peroxotungstate $CaWO_6 \cdot H_2O$ is a true peroxide. The more intense dehydration of $CaWO_6 \cdot H_2O$ over a long time led to the formation of a product containing 0.5-0.4 mole of water and 0.5 mole of peroxide O_2 per gram ion of calcium, which corresponds to the formula $CaWO_5 \cdot 0.5 H_2O$. These experiments afford a basis for supposing that in the course of dehydration the probability of transition of the peroxo form to the peroxy form is not excluded and that the compound $CaWO_6 \cdot H_2O$ may have an isomeric form of the composition $CaWO_5 \cdot H_2O_2$.

The yellow product of the composition $CaWO_6 \cdot nH_2O$ behaved uniquely on dehydration: the ratio of the number of moles of $CaWO_4$ to O_2 in it was maintained at 1 : 2 while $n \geq 8$; upon being kept in the refrigerator it lost 0.25-0.3 mole of peroxide oxygen. The loss of the indicated amount of peroxide O_2 took place during continuous drying of the product over P_2O_5 .

With a water content from 8 to 3 moles, the ratio of the number of moles of $CaWO_4$: O_2 was 1 : 1.75, which corresponds to the formula $CaWO_{7.5} \cdot 3H_2O$ or $2CaWO_7 \cdot 5H_2O_2$. The product of such composition could be stored in the refrigerator for a rather long time. Further dehydration of $CaWO_{7.5} \cdot 3H_2O$ was obviously retarded. Upon de-

TABLE 1. Temperatures to which the Extreme Points on the Thermograms of the Compounds Investigated Correspond

Compound	Exothermic effect	Endothermic effect	Beginning of maximum
$\text{CaWO}_6 \cdot n\text{H}_2\text{O}$	46°	102°	44°
$\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$	67	106	46
$\text{CaWO}_6 \cdot \text{H}_2\text{O}$	75	Inconspicuous ~ 120	70

hydration or even upon slight heating, $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ and $\text{CaWO}_{7.5} \cdot 3\text{H}_2\text{O}$ loss peroxide oxygen simultaneously with the loss of water.

The observations carried out lead to the conclusion that the yellow peroxides are peroxyhydrates of the white lower peroxo compounds, and consequently they must be regarded as the mixed peroxooxy compounds $2\text{CaWO}_6 \cdot 3\text{H}_2\text{O}_2 \cdot 3\text{H}_2\text{O}$ and $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}_2 \cdot 6\text{H}_2\text{O}$.

Thermographic Observations

The basis for a broad thermographic investigation of the peroxides was laid by the research of S. Z. Makarov et al. [3].

The calcium peroxotungstates $\text{CaWO}_6 \cdot \text{H}_2\text{O}$, $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$, and $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ were subjected to thermographic observation with the photorecording pyrometer of N. S. Kurnakov. Chemically pure potassium bichromate served as the standard. A weighed sample of about 0.2-0.4 g of the product was used. The temperature was measured with a copper-constantan thermocouple. Measurement of the temperature was carried out over the course of 100-120 minutes. Parallel experiments showed satisfactory agreement of the results.

The thermograms for these products have a maximum and minimum (Table 1); consequently, for each product they show the presence of two effects—exothermic and endothermic.

The exothermic effect is associated with the destruction of the peroxide groups, and the endothermic is due to the removal of water.

The data in Table 1 permit the assumption that all three products have the same basic core of peroxide nature, most likely CaWO_6 .

For $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ at a temperature of about 58-60° there is a small second exothermic effect, which is a supplement or prolongation of the first. This fact confirms the previous conclusion that in the yellow higher peroxides the nature of the peroxides groups is not the same; in other words, the yellow products contain peroxo and peroxy groups.

The maxima for $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$ and particularly for $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ are considerably higher than for $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ and, as can be seen from the data of Table 1, the beginning of the maximum for the last-named compound corresponds to a different temperature than for the first two.

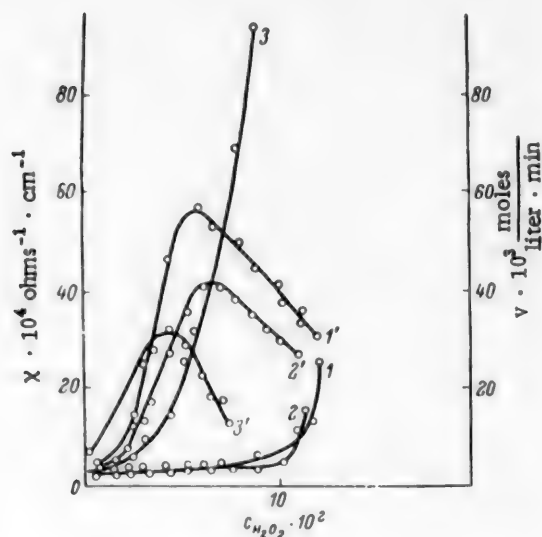
To interpret the thermograms, the calcium peroxotungstates were placed in quartz test tubes connected with a volumeter and were heated at the temperatures indicated in Table 1. The contents of the test tubes were analyzed for peroxide oxygen, water, and dry residue; the last in all cases represented normal calcium tungstate. These experiments showed agreement with the data obtained by thermographic investigation of the compounds.

Relation of the Properties of the Peroxo Salt to the Difference in Its Water Content

The white calcium peroxotungstate $\text{CaWO}_6 \cdot n\text{H}_2\text{O}$ was first dehydrated to a value of n equal to 3, 2, 1, and even less than 1, then specific gravities were determined for these hydrates, the kinetics of their decomposition and their electroconductivity were studied, and the heat effects of decomposition were determined.

The specific gravities were determined in a pycnometer with carbon tetrachloride. The following values were obtained for the specific gravities: for $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$ d 4.3892; for $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$ d 4.3205; for $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ d 4.3330. With a decrease in the water content of the molecule of the peroxide the specific gravity increased.

The kinetics of decomposition and the electroconductivity of the peroxohydrates were investigated in aqueous solution. It might seem that the products that had been dehydrated to different degrees should on contact with water be hydrated and as a result of this the kinetic curves for $\text{CaWO}_6 \cdot \text{H}_2\text{O}$, $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$, and $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$ should be superimposed on one another; similarly the value of the electroconductivity for all these hydrates in solution should be the same. Our experiments, however, showed an entirely different picture than might be expected. In the figure shown, the values represented on the ordinate axis are: v , the rate of decomposition expressed in moles/liter \cdot min of oxygen evolved, and κ , the specific electroconductivity in $\text{ohms}^{-1} \cdot \text{cm}^{-1}$; on the abscissa axis is c , the concentration of the peroxohydrate in moles/liter calculated as H_2O_2 . The volume of the reaction mixture in all cases was 40 ml.



Relation of electroconductivity and rate of decomposition of CaWO_6 to different water content of the molecule of the starting compound. At 35° : 1, 1') $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$; 2, 2') $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$. At 0° : 3, 3') $\text{CaWO}_6 \cdot \text{H}_2\text{O}$.

type of recombination of the peroxide oxygen atoms on reaction with the solvent in comparison with the peroxohydrates for which $n \geq 2$.

If the decomposition of the peroxides at $n \geq 2$ is of consecutive nature and considerable amounts of free H_2O_2 are formed in solution, then the decomposition of $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ to the normal salt is completed almost at one stroke. Free H_2O_2 here is formed in relatively small amount. As a result of the fact that the lower intermediate peroxide and free H_2O_2 are formed much more easily from the more hydrated peroxohydrates, the break in the kinetic curve for the decomposition of $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ occurs at the end of the experiment, while for the other peroxohydrates the break is observed at the beginning of the process.

Experiments carried out showed directly how great an effect the degree of hydration and peroxyhydration of the intermediate products have on the decomposition constant of these compounds during catalysis in solutions [2].

Determination of Thermal Effects of Decomposition of Calcium Peroxotungstates

For the determination of the thermal effects of decomposition of the calcium peroxotungstates their reaction with potassium permanganate in acid medium was employed. This method had been used previously for thermochemical investigations of peroxides [4, 5]. In reference [5] the methods of thermochemical investigation are described in detail.

The experiments were carried out in an adiabatic calorimeter using an accurate electromeasuring apparatus. Correction was made for radiation in all the experiments by Bunte's formula. The error of the experiments did not exceed 1.5%.

Most frequently a sample of about 0.5 g of the yellow product and about 1 g of the white product was used; $c_{\text{H}^+} = c_{\text{KMnO}_4} = 0.1 \text{ N}$. The elevation in temperature was $0.4\text{--}0.6^\circ$.

The thermal effect Q which was sought for the decomposition of the calcium peroxotungstates was calculated by Hess' law $Q = Q_2 - Q_3 - Q_1$. The values of the thermal effects of the reaction of H_2O_2 with KMnO_4 (Q_1) and of the

It is seen from the figure that the curves for the change in electroconductivity (Curves 1', 2', 3') have a maximum, and the greater the water content of the product, the more clearly this maximum is expressed. The absolute value of the electroconductivity increases with an increase in the number of moles of H_2O in the peroxohydrate.

The kinetic curves 1 and 2 are superimposed on each other, i.e., at $n \geq 2$ the presence of the water does not exert any effect on the nature of the kinetic curves nor on the absolute rate of decomposition of the product in solution. At $n \leq 1$ the product decomposes in solution at 35° so violently that investigation of it at this temperature proved impossible. Even at 0° , as kinetic curve 3 shows, the rate of decomposition of $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ was many times greater than that of $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$ and $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$ at 35° . From this it follows that $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ has a special structure and a different

TABLE 2. Thermal Effects of Decomposition of Calcium Peroxotungstates

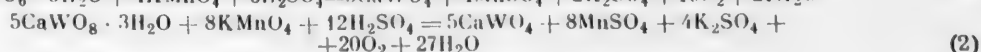
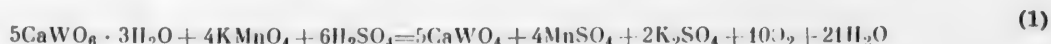
Peroxo salt	Q (Kcals/ mole)
$\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$	39.10
$\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$	26.77
$\text{CaWO}_6 \cdot \text{H}_2\text{O}$	11.68
$\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$	59.44

decomposition of H_2O_2 to H_2O and O_2 (Q_2) were 147.1 and 90.88 kcals/mole respectively. We determined Q_3 experimentally as the thermal effect of the reaction of the calcium peroxotungstates with KMnO_4 in acid medium. The data obtained are given in Table 2.

It can be seen that the thermal effect of decomposition of $\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$ is much greater than that of $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$.

The experiments carried out revealed rather interesting facts. It turned out that calcium peroxotungstate, depending on the amount of water of hydration contained in it, reacts with potassium permanganate in different ways. When the peroxides with the composition

$\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$, $\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$, $2\text{CaWO}_7 \cdot 5\text{H}_2\text{O} \cdot \text{H}_2\text{O}$, and $\text{CaWO}_8 \cdot n\text{H}_2\text{O}$ react with KMnO_4 , the amount of oxygen given off corresponds to the following reactions:



$\text{CaWO}_6 \cdot \text{H}_2\text{O}$ behaves entirely differently in acid solution of permanganate. The amount of O_2 given off in this case is approximately 1/2.1 that which should be obtained in an oxidizing-reducing reaction of $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ with KMnO_4 .

In this case the amount of O_2 given off corresponds approximately to the reaction $\text{CaWO}_6 \cdot \text{H}_2\text{O} \rightarrow \text{CaWO}_4 + \text{O}_2 + \text{H}_2\text{O}$ (3).

The process of decomposition of this product is completed very rapidly. Consequently $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ behaves in permanganate solution the same as in pure water. Calcium peroxotungstate of the composition $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$ possibly reacts according to reaction (1) and partially according to scheme (3). Therefore the values of Q given in Table 2 for $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ and $\text{CaWO}_6 \cdot 2\text{H}_2\text{O}$ are the minimum thermal effects for their decomposition, while the values of Q for $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$ and $\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$ are true ones.

Taking into consideration the fact that $\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$ reacts mainly according to scheme (3), we can calculate the thermal value for this product directly without using Hess' law. It is 37.4 kcals/mole. The value obtained for the heat of decomposition of $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ is very approximate.

On the basis of the thermal effects obtained, the values for the bond energy of the peroxide oxygen with WO_4^{2-} were calculated and were found to be 43.64, 38.95 and 39.80 kcals/mole for $\text{CaWO}_8 \cdot 3\text{H}_2\text{O}$, $\text{CaWO}_6 \cdot 3\text{H}_2\text{O}$, and $\text{CaWO}_6 \cdot \text{H}_2\text{O}$, respectively.

In conclusion it should be noted that the thermochemical investigations have shown the usefulness of the indirect method employing potassium permanganate to determine the thermal effects of decomposition of the most highly hydrated calcium peroxotungstates.

The experiments carried out confirm the idea that the peroxo compounds decompose most rapidly not through reciprocal deoxidation of the peroxides (which in general is not excluded), but by direct splitting off of oxygen from the molecule of the peroxide compound.

In the process of dehydration of the peroxides the nature of addition of the peroxide O_2 in the molecule of the basic compound changes and therefore its structure and properties become different. The greater the water content of the molecule of the compound, the more easily it forms peroxyhydrates in solution.

In conclusion we express our hearty thanks to I. A. Pusinov for making the thermographic measurements.

SUMMARY

1. The complete composition of the calcium peroxotungstates has been determined. The yellow peroxides are mixed peroxy compounds, and the white $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ is a true peroxide.
2. It has been demonstrated that dehydration can essentially change the properties and structure of peroxides. The less water the calcium peroxotungstate contains, the greater is its rate of decomposition and the less its elec-

troconductivity. It has been established that $\text{CaWO}_6 \cdot \text{H}_2\text{O}$ differs sharply from the other hydrates and does not react with KMnO_4 like an ordinary peroxide, but decomposes in it, as it does in water, to CaWO_4 and O_2 .

3. Thermographic investigations have shown that for each of the calcium peroxotungstates there are two thermal effects – an exothermic one associated with the destruction of the peroxide groups, and an endothermic one due to the removal of water.

4. The thermal effects of decomposition and the specific gravities have been determined for the calcium peroxotungstates.

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DIAMAGNETIC SUSCEPTIBILITY OF INTERNAL COMPLEXES OF MOLYBDENUM

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Original article submitted June 13, 1960

Compounds of hexavalent molybdenum, if they do not contain any other paramagnetic center, as a rule are diamagnetic or have weak paramagnetism independent of temperature. This fact is explained by the circumstance that hexavalent molybdenum does not contain unpaired electrons. A study of the magnetic susceptibility of internal complexes of molybdenum (VI) is of interest because up to now the magnetic properties of compounds of hexavalent molybdenum with organic materials have not been investigated.

Experimental and Calculated Values of the Magnetic Susceptibility of Internal Complexes of Molybdenum

Compound	Susceptibility of complex			$(\chi_{\text{calc.}} - \chi_{\text{expt.}}) \cdot 10^6$
	specific	molar		
		$\chi_{\Gamma} \cdot 10^6$	$\chi_{\text{expt}} \cdot 10^6$	
Molybdenyl salicylalanilate ($\text{C}_{25}\text{H}_{10}\text{ON}_2$) $_2\text{MoO}_2$	-0.388	-202.0	-216.0	-14.0
Molybdenyl salicylal-m-nitro-anilate ($\text{C}_{13}\text{H}_9\text{O}_3\text{N}_2$) $_2\text{MoO}_2$	-0.393	-236.0	-234.0	+2.0
Molybdenyl salicylal- β -naphthal-amine ($\text{C}_{17}\text{H}_{12}\text{ON}$) $_2\text{MoO}_2$	-0.471	-295.0	-279.0	+16.0
Molybdenyl salicylal-p-anisidinate ($\text{C}_{14}\text{H}_{12}\text{O}_2\text{N}_2$) $_2\text{MoO}_2$	-0.380	-220.0	-231.0	-11.0
Molybdenyl 2-hydroxy-1-naphthalanilate ($\text{C}_{17}\text{H}_{12}\text{ON}$) $_2\text{MoO}_2$ *	-0.550	-385.0	372.0	+13.0
Molybdenyl 2-hydroxy-1-naphthal-p-nitroanilate ($\text{C}_{17}\text{H}_{11}\text{O}_3\text{N}_2$) $_2\text{MoO}_2$	-0.440	-352.0	-355.0	-3.0
Molybdenyl 2-hydroxy-1-naphthal-p-anisidinate ($\text{C}_{18}\text{H}_{14}\text{O}_2\text{N}_2$) $_2\text{MoO}_2$	-0.460	-314.0	-308.0	+6.0
Molybdenyl 2-hydroxy-1-naphthal-p-iodoanilate ($\text{C}_{17}\text{H}_{11}\text{ONI}$) $_2\text{MoO}_2$	-0.388	-342.0	-350.0	-8.0
Molybdenyl 2-hydroxy-1-naphthal-o-methoxyanthranilate ($\text{C}_{18}\text{H}_{14}\text{O}_3\text{N}_2$) $_2\text{MoO}_2$	-0.420	-310.0	322.0	-12.0

* As in Russian. Publishers note.

It naturally was expected that the internal complexes of molybdenum with Schiff bases which we synthesized [1] would be diamagnetic. The synthesis of these internal complexes was accomplished by reaction of ether or benzene solutions of the Schiff base with an ether solution of molybdenum oxychloride.

The nature of the reaction of the molybdenum with the ligands in the internal complexes investigated is in general little changed from one Schiff base to another, since the latter here have the same type of structure. It therefore is possible to compare the experimental values of the magnetic susceptibility with those calculated by the old magnetochemical scheme of Pascal; the molar magnetic susceptibility of the internal complex can be considered equal to the sum of the susceptibilities of the molybdenum ion and the ligands.

From the literature [2] it is known that the susceptibility of molybdenum oxychloride is $\chi_{\text{MoO}_2\text{Cl}_2} = -22 \cdot 10^{-6}$. Taking the susceptibility of the chlorine as $\chi_{\text{Cl}} = -20.1 \cdot 10^{-6}$ [3], we find the susceptibility of the molybdenum ion, which is $+18 \cdot 10^{-6}$. The susceptibility of the ligands was calculated by the old scheme of Pascal, which in spite of the absence of a strict physical basis, gives results that agree well with the experimental.

The new magnetochemical scheme recently proposed by Ya. G. Dorfman [4, 5] for the calculation of the diamagnetic susceptibility of organic compounds has a theoretically firm basis, but it has been used thus far only for aliphatic and alicyclic compounds. Furthermore, the magnitude of the polarization paramagnetism of the magnetophoric group $>\text{C}=\text{N}-$, which occurs in the Schiff bases, remains unknown. We therefore could not calculate the diamagnetic susceptibility of the internal complexes under investigation by Dorfman's method, which no doubt would be of great interest.

The magnetic susceptibility of nine internal complexes of hexavalent molybdenum were measured by the method of Guy at room temperature. The results of the measurements are given in the table, from which it can be seen that the calculated molar susceptibilities of the molybdenum complexes agree satisfactorily with the experimental values. The deviations between these values apparently is of a chance nature and is explained by experimental errors.

SUMMARY

The diamagnetic susceptibility of nine internal complexes of hexavalent molybdenum has been measured.

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SYNTHESIS OF SOME GUANYLS OF SULFONIC ACIDS

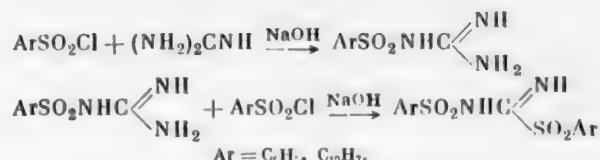
D. F. Kutenov, D. N. Khokhlov, and V. L. Tuzhilkina

Translated from *Zhurnal Obshchei Khimii*, Vol. 31, No. 9,

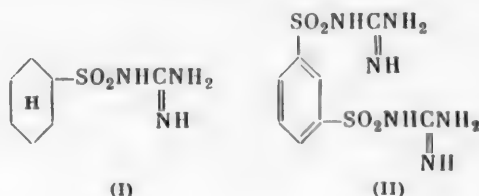
p. 2825, September, 1961

Original article submitted December 24, 1960

A general method of preparing guanyls of sulfonic acids is the condensation of the acid chlorides of these acids with guanidine in the presence of alkalis [1-3].



In studying the reaction of guanidine with α -diketones [4], when the appropriate sulfonyl chloride was reacted with guanidine, we obtained cyclohexanesulfoguanyl (I) and m-chlorobenzenedisulfodiguanyl (II), which have not been described in the literature.



EXPERIMENTAL

Cyclohexanesulfoguanyl (I). To a solution of 5 g of guanidine carbonate and 3.6 g of sodium hydroxide in 20 ml of water was added in portions 5.1 g of cyclohexanesulfonyl chloride. The flask was shaken vigorously for 7-10 minutes, after which the precipitate that had settled out was filtered off and washed with water, alcohol, and ether. It was recrystallized from water. M.p. 290-290.5° (decomp.).

Found %: C 41.30; H 7.51; N 20.36. $\text{C}_7\text{H}_{15}\text{O}_2\text{N}_3\text{S}$. Calculated %: C 40.99; H 7.33; N 20.29.

m-Benzenedisulfodiguanyl (II). A mixture of 5 g of m-benzenesulfonyl chloride and 2.5 g of guanidine carbonate was triturated in a mortar and heated to 100°, whereupon the mixture melted with the evolution of gas. The cooled melt was dissolved in hot alcohol, ether was added to the solution, and it was cooled with ice water. The white precipitate that settled out was separated and recrystallized from isopropyl alcohol. M.p. 202°.

Found %: N 19.90; S 14.15. $\text{C}_8\text{H}_{12}\text{O}_4\text{N}_6\text{S}_2 \cdot 2\text{H}_2\text{O}$. Calculated %: N 19.20; S 14.90.

SUMMARY

Cyclohexanesulfoguanyl and m-benzenedisulfodiguanyl have been synthesized.

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PREPARATION OF SUBSTITUTED ACIDS THROUGH THE FURAN DERIVATIVES

V. SYNTHESIS OF D,L-PROLINE

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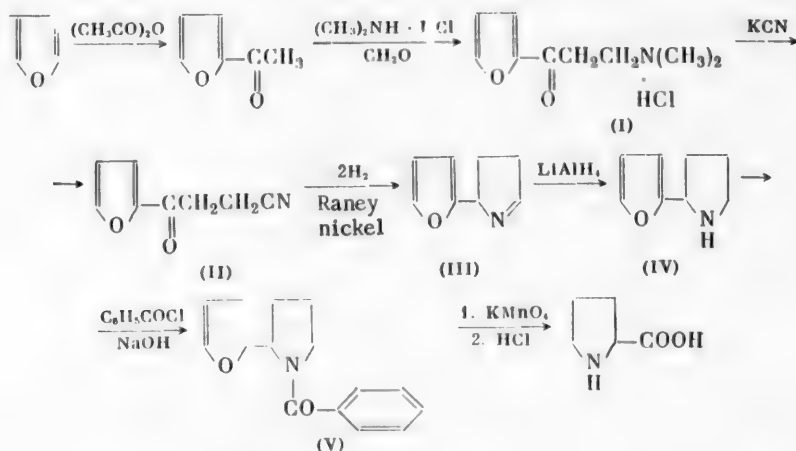
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In previous communications [1-3] it has been shown that when benzoyl derivatives of amines of the furan series are oxidized, benzoyl derivatives of the amino acids are formed. Monobasic α - and γ -amino acids (in the form of the benzoyl acids) and aspartic acid have been prepared.

In the present work we employed the same route for the preparation of a cyclic amino acid, proline, by the following scheme:



α -Acetofuran was prepared by acylation of furan in the presence of boron trifluoro etherate [4, 5]. Use of the Mannich reaction for ketones of the furan series has received comparatively little study. Aminomethylation of aceto-furan has been described in the literature [6], but the yield of the hydrochloride obtained was not indicated. We prepared β -(α -furyl) dimethylaminoethyl ketone in the form of the hydrochloride in 68% yield. We converted the hydrochloride of β -(α -furyl) dimethylaminoethyl ketone to (α -furoyl)- β -propionitrile (II) by boiling an aqueous solution of the hydrochloride of the Mannich base with a double excess of potassium cyanide in acetate buffer and in a current of nitrogen and obtained the pure crystalline nitrile (II) in 70% yield. 2-Furylpyrroline (III) was obtained in 37% yield by hydrogenation of (α -furoyl)- β -propionitrile with hydrogen in the presence of Raney nickel at room temperature and atmospheric pressure [8]. We tried to convert 2-(α -furyl)pyrroline (III) to 2-(α -furyl)pyrrolidine (IV) under similar conditions, but it turned out that this reaction goes very slowly and a mixture of two compounds is formed, the separation of which presents considerable difficulties. We reduced the double bond in 2-(α -furyl)pyrroline with lithium aluminum hydride and obtained 2-(α -furyl)pyrrolidine in 85% yield. Oxidation of N-benzoyl-2-(α -furyl)pyrrolidine was carried out with twice the theoretical amount of potassium permanganate in alkaline medium; the N-benzoyl-D,L-proline obtained was hydrolyzed (without isolation) by boiling with dilute hydrochloric acid. The total yield of the two last stages combined was 61.7% (formol titration). Free racemic proline was isolated with the aid of ion exchange resin KU-2. The total yield of proline calculated on the basis of the starting furan was about 14%.

EXPERIMENTAL

β -(α -Furyl) dimethylaminoethyl ketone (I). To a mixture of 80 g of acetofuran, 22 g of paraform, 58 g of dimethylamine hydrochloride, and 150 ml of anhydrous alcohol was added 4-5 drops of concentrated hydrochloric acid and the mixture was boiled for 2 hours. The white crystalline precipitate that separated out upon cooling was filtered off and dried. One hundred grams (66.5%) of the hydrochloride of (I) was obtained with m.p. 177-178° (from water) [6].

β -(α -Furoyl)propionitrile (II). To a mixture of 81.5 g of (I) and 52 g of potassium cyanide was added 2850 ml of boiling buffer prepared from the calculated amount of 6 g of acetic acid and 8.5 g of sodium acetate per liter of water. The solution was refluxed in a current of nitrogen for 30 minutes. After cooling, yellow crystals precipitated. The filtrate after separation of the precipitate was extracted with chloroform, the solution was dried with magnesium sulfate, and the chloroform was distilled off. Another 20.5 g of nitrile (II) was obtained. A total of 41.9 g (70.7%) was obtained with m.p. 75-76° (from alcohol) [7].

2-(α -Furyl)pyrroline (III). A solution of 5 g of β -(α -furoyl)propionitrile in 70 ml of methyl alcohol was hydrogenated in the presence of 2 g of Raney nickel. Six hours, after the absorption of 1.5 liters of hydrogen, the hydrogenation was stopped and the catalyst was filtered out and washed with 10 ml of methyl alcohol. After distillation of the solvent, the 2-(α -furyl)pyrroline remained in the form of a yellow oil which upon cooling crystallized completely. Yield 3.9 g (87%), m.p. 55-56° (from petroleum ether); picrate, m.p. 176-177° (from alcohol) [8].

2-(α -Furyl)pyrrolidine (IV). To a vigorously stirred mixture of 4 g of lithium aluminum hydride in 100 ml of ether at -10° was added over 45 minutes a solution of 3.9 g of 2-(α -furyl)pyrroline (III) in 50 ml of absolute ether. The cooling was stopped and the mixture was brought to room temperature and refluxed for 4 hours. The residue of lithium aluminum hydride was decomposed with a saturated solution of potassium carbonate. The ether layer was separated, the residue was washed three times with ether, and the combined ether extracts were dried with fused potassium hydroxide. The 2-(α -furyl)pyrrolidine (3.7 g) was obtained in the form of an oil. Yield 85%. Picrate, m.p. 155°. Benzoyl derivative, m.p. 72-73° (from petroleum ether), yield quantitative.

Found %: C 74.69, 74.60; H 6.58, 6.47; N 5.80, 5.55. $C_{15}H_{15}O_2N$. Calculated %: C 74.68; H 6.39; N 5.80.

D,L-Proline. To a solution of 1.5 g of N-benzoyl-2-(α -furyl)pyrrolidine in 30 ml of acetone was added 1 ml of 20% potassium hydroxide solution. The vigorously stirred mixture was cooled to 5-10°, a solution of 12.3 g of potassium permanganate in 200 ml of water was added gradually, and the mixture was stirred for 4 hours and left overnight. The manganese dioxide that had precipitated out was filtered off, the filtrate was evaporated in vacuum, and the dry residue was extracted with ether, dissolved in 60 ml of water, and boiled with carbon. To the filtrate was added 3 ml of concentrated hydrochloric acid and the mixture was boiled for 6 hours. After cooling, the benzoic acid that had precipitated was filtered off and the filtrate was extracted three times with ether. In the filtrate 0.429 g (61.7%) of proline was detected by formol titration. The filtrate was passed through a column with cation exchange resin KU-2, the resin was washed with distilled water until there was a negative reaction for chlorine, and the proline was eluted with 5% ammonia solution. After evaporation 0.4 g of D,L-proline was obtained with m.p. 203-204° (from anhydrous alcohol) [9]; R_f 0.61 (pyridine : water = 80 : 20).

SUMMARY

A method has been developed for the preparation of racemic proline from furan.

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AROMATIC HYDROCARBONS

XX. CHRYSENE

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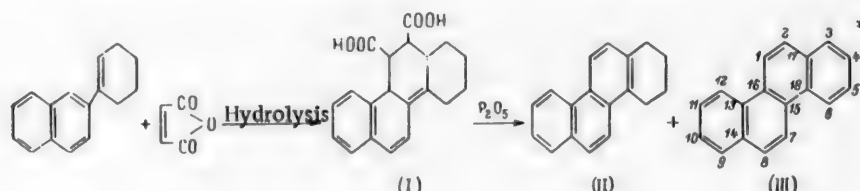
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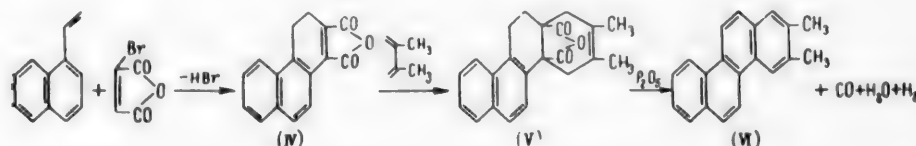
In the present work the possibility has been investigated for using the reaction between phosphorus pentoxide and adducts of the diene synthesis [1] for the preparation of chrysene and its homologs.

For the synthesis of chrysene (III), we subjected to heating with phosphorus pentoxide the 1,2,3,4,5,6,16,17-octahydrochrysenedicarboxylic-1,2 acid (I), which in turn had been prepared by the hydrolysis of the adduct of β -cyclohexenylnaphthalene with maleic anhydride. It appeared that the acid (I) broke down only upon prolonged (6-7 hours) gradual heating in a metal bath from 210 to 350°, forming (in ~20% yield) 3,4,5,6-tetrahydrochrysene* (II), which was identified by its melting point and the melting point of the picrate, and also by dehydrogenation to chrysene. Besides the tetrahydrochrysene, we isolated from the products of the reaction with phosphorus pentoxide a small amount of chrysene (III), the formation which was due (as shown by analysis of the gas evolved) to the processes of dehydrogenation and also of decarboxylation that occurred simultaneously with the decarbonylation.



Chrysene (III) was identified by its melting point and the melting point of the product of addition of 1,3,5-trinitrobenzene, and also by its absorption spectrum in the UV region, which agreed fully with the literature data [2].

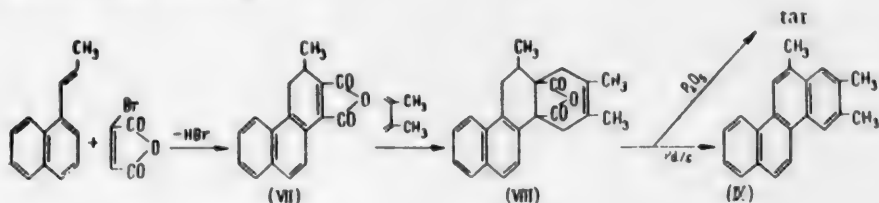
For the synthesis of 4,5-dimethylchrysene (VI) we reacted the anhydride of 4,5-dimethyl-1,2,3,6-tetrahydrochrysenedicarboxylic-17,18 acid (V) with phosphorus pentoxide. This anhydride (V) was prepared by a double diene synthesis: by the reaction of α -vinyl-naphthalene with bromomaleic anhydride (by heating in glacial acetic acid in a stream of nitrogen) the anhydride of 3,4-dihydrophenanthrenedicarboxylic-1,2 acid (IV) was obtained, which was further used for a diene synthesis with 2,3-dimethylbutadiene-1,3 in the presence of picric acid and phenothiazine. From the products of the reaction of the anhydride (V) with phosphorus pentoxide we isolated only 4,5-dimethylchrysene (VI) (39% yield)(identified by analysis).



Thus the intermediately formed 4,5-dimethyldihydrochrysene was immediately and completely dehydrogenated under the reaction conditions, while tetrahydrochrysene (II) was only partially dehydrogenated.

* The numbering of the carbon atoms is that employed in Elsevier's encyclopedia.

The synthesis of 2,4,5-trimethylchrysene (IX) was accomplished by a similar scheme, using as the starting diene hydrocarbon α -propenylnaphthalene instead of α -vinylnaphthalene. We obtained by the same double diene synthesis procedure the anhydride of 2,4,5-trimethyl-1,2,3,6-tetrahydrochrysenedicarboxylic-17,18 acid (VIII), but upon heating this anhydride with phosphorus pentoxide, in contrast to the anhydride (V), extensive tar formation occurred (the gas formed contained carbon dioxide), and we did not succeed in isolating 2,4,5-trimethylchrysene. The anhydride (VIII) was converted to 2,4,5-trimethylchrysene (IX) in 66% yield only by heating to 330-340° in the presence of a catalyst (palladium on carbon).



EXPERIMENTAL

Chrysene

β -Cyclohexenylnaphthalene was prepared by dehydration by heating with potassium bisulfate of the alcohol synthesized by reaction of β -naphthylmagnesium bromide with cyclohexanone [3]. M.p. 61.5-62° (from alcohol), yield 38%.

Adduct (I) from β -cyclohexenylnaphthalene and maleic anhydride. Fifteen grams of β -cyclohexenylnaphthalene and 75 g of maleic anhydride were refluxed for 20 hours on a water bath. The reaction mixture was dissolved in 2 N alkali solution, the unreacted diene was extracted with benzene, the alkaline solution was acidified, the precipitate that separated out was filtered off and again purified by dissolving it in alkali and precipitating with acid: m.p. 225-230° (this adduct has been described in the literature [3], isolated in the form of the anhydride with m.p. 216°).

Reaction of adduct (I) with phosphorus pentoxide was carried out by refluxing on an oil bath (230-350°) for 6-7 hours until the evolution of gas ceased. The 3,4,5,6-tetrahydrochrysene (II) produced (from 40 g of adduct (I) and 19 g of phosphorus pentoxide 5.5 g, 20%, was obtained) sublimed during the reaction process from the reaction mixture and gradually collected in the lower part of the reflux condenser. After heating with alkali to remove possible contamination by the starting adduct and recrystallization from acetic acid, the tetrahydrochrysene (II) melted at 183-184°; picrate, m.p. 133-134° (from benzene) [4].

Chrysene (III) was isolated from the reaction mixture in the following manner: after the conclusion of heating with phosphorus pentoxide the reaction mixture was extracted by heating with butyl alcohol or toluene; the residue obtained after distilling off the solvent from the combined extracts was boiled with alkali, filtered, washed with water, dried, then dissolved in dry toluene and purified by passing through a column with alumina. The chrysene purified in this way (1.2 g) was again recrystallized from toluene or xylene, m.p. 250°; complex with 1,3,5-trinitrobenzene, m.p. 188-189° (from benzene) [5, 6].

The gas evolved during the reaction contained 47% CO, 27% CO₂, 11% H₂, and 14% unsaturated hydrocarbons.

4,5-Dimethylchrysene

Anhydride of 3,4-dihydrophenanthrenedicarboxylic-1,2 acid (IV). α -Vinylnaphthalene (15.4 g) and bromo-maleic anhydride (35.4 g) in glacial acetic acid (10 ml) were refluxed for 12 hours in a current of nitrogen; the next day the precipitate that had separated out was filtered off, washed with benzene and with acetone, and recrystallized from dioxane. M.p. 271-271.5° [7]. Yield 8.8 g (35%).

Adduct (V) from anhydride (IV) and 2,3-dimethylbutadiene-1,3. Four grams of anhydride (IV), 4 ml of freshly distilled 2,3-dimethylbutadiene-1,3, and 35 ml of dioxane were heated in the presence of phenothiazine and picric acid (0.1 g each) for 24 hours in an autoclave at 160-170°; the residue after the solvent was distilled off was washed with a small amount of benzene - petroleum ether mixture (1 : 1). Yield of adduct (V) 3.5 g (66%), m.p. 196-196.8° (from cyclohexane) [8].

Reaction of adduct (V) with phosphorus pentoxide. Four grams of adduct (V) and 1.8 g of phosphorus pentoxide were heated for 1.5 hours on a metal bath from 210 to 260° and the reaction mixture was extracted with benzene; the benzene solution was boiled with alkali. The residue after the benzene was distilled off was sublimed in vacuum

(2-3 mm) and recrystallized from benzene. The hydrocarbon thus obtained (1.25 g, 40%) melted at 208-209°; after several recrystallizations from alcohol the melting point remained constant. Since according to the data in the literature [9] 4,5-dimethylchrysene melts at 215-215.3°, the hydrocarbon obtained was heated at 340° in the presence of palladium on carbon (to dehydrogenate possible contaminating dimethyldihydrochrysene), but in this case also its melting point was unchanged, and the analytical data corresponded to dimethylchrysene.

Found %: C 93.52, 93.62; H 6.43, 6.33. $C_{20}H_{18}$. Calculated %: C 93.7; H 6.3.

2,4,5-Trimethylchrysene

Anhydride of 3-methyl-3,4-dihydrophenanthrenedicarboxylic-1,2 acid (VII). α -Propenylaphthalene (13.5 g), bromomaleic anhydride (21.5 g), glacial acetic acid (10 ml), picric acid, and phenothiazine (0.1 g each) were refluxed for 0.5 hour in a flask and left overnight. The next day the precipitate was filtered off, washed with a mixture of benzene and petroleum ether (1 : 3), and dried in a vacuum desiccator. M.p. 188-188.5° (from acetic acid), yield 9.1 g (43%). The anhydride (VII) obtained was easily dehydrogenated by heating to the anhydride of 3-methylphenanthrenedicarboxylic-1,2 acid with m.p. 308°.

Found %: C 77.79, 77.85; H 4.03, 4.07. $C_{17}H_{10}O_3$. Calculated %: C 77.85; H 3.84.

Adduct (VIII) from the anhydride (VII) and 2,3-dimethylbutadiene-1,3 was obtained under conditions similar to those used in the preparation of adduct (V). From 5 g of anhydride (VII) we obtained 2.4 g (37%) of adduct (VIII), m.p. 176.5° (from petroleum ether-benzene mixture, 1 : 1).

Found %: C 79.74, 79.50; H 6.57, 6.52. $C_{23}H_{22}O_3$. Calculated %: C 79.74; H 6.40.

The anhydride of 3-methylphenanthrenedicarboxylic-1,2 acid, the product of dehydrogenation of the starting anhydride (VII), also was isolated with m.p. 308°.

Aromatization of adduct (VIII). Adduct (VIII) (0.5 g) and 20% palladium catalyst (1 g) on carbon were heated for 45 minutes at 330-340° and the 2,4,5-trimethylchrysene (IX) which was produced was distilled off in vacuum; yield 0.25 g (66%), m.p. 126-127° (from benzene-petroleum ether mixture).

Found %: C 93.19, 93.00; H 6.97, 7.03. $C_{21}H_{18}$. Calculated %: C 93.26; H 6.71.

Picrate, m.p. 202-203° (from alcohol-acetone mixture, 2 : 1).

Found %: N 7.97, 8.27. $C_{21}H_{18} \cdot C_6H_3O_7N_3$. Calculated %: N 8.09.

SUMMARY

Aromatization of adducts of the diene synthesis under the influence of phosphorus pentoxide has been employed to prepare tetrahydrochrysene, chrysene, and 4,5-dimethylchrysene. 2,4,5-Trimethylchrysene could not be obtained in this way; it was prepared by catalytic aromatization of the adduct of diene synthesis over palladium on carbon.

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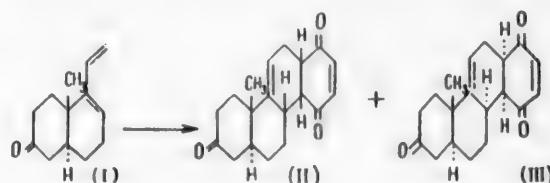
AN INVESTIGATION OF THE STEREOCHEMISTRY
OF CYCLIC COMPOUNDS

XL. THE STEREOCHEMISTRY OF THE DIENE CONDENSATION OF TRANS-
1-VINYL-6-KETO-9-METHYL- Δ^1 -OCTALIN WITH MALEIC ANHYDRIDE
AND SOME TRANSFORMATION OF THE ISOMERS WITH ARE FORMED
AND OF THEIR KETALS

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As was shown in one of the preceding communications [1], the condensation of trans-1-vinyl-6-keto-9-methyl- Δ^1 -octalin (I) with quinone proceeds nonselectively and leads to a mixture of the geometric isomers (II) and (III), the configurations of which were confirmed by a series of stereospecific transformations. The basic stereochemical feature of this reaction is the intermediate formation of the endoadduct (II), which arises as a result of the addition of the quinone to the diene from the side opposite the angular methyl group of the latter.

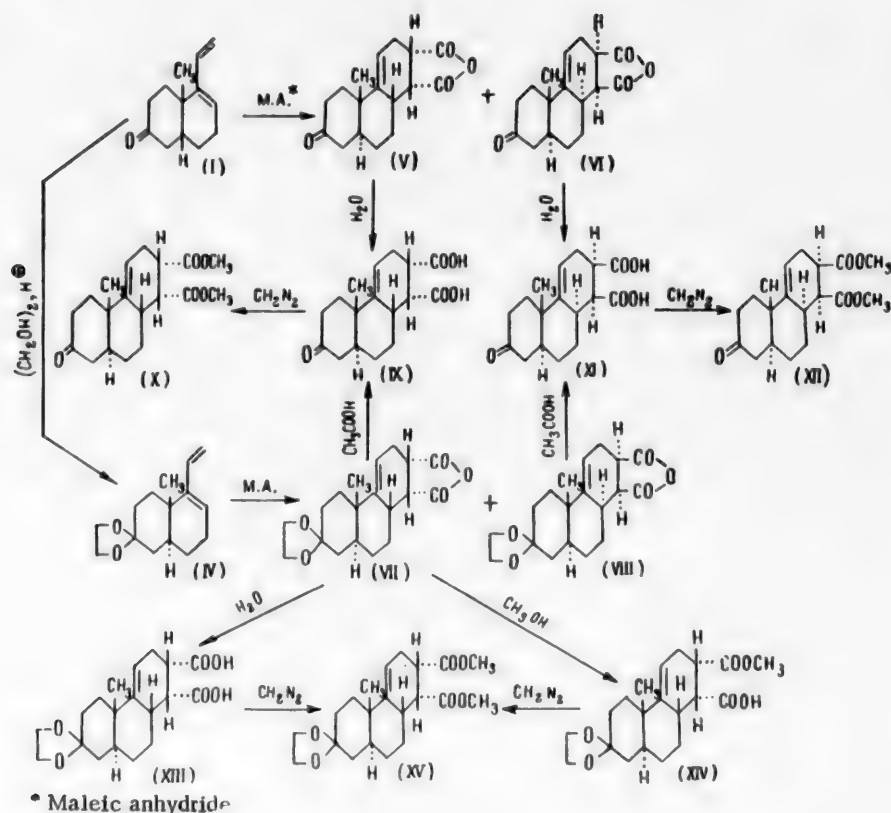


It appeared interesting to study the stereochemistry of the parallel reactions with maleic anhydride. The tricyclic-o-dicarboxylic acids which are formed by this are models for the A and B rings of the allosterooids and can be used in the future both for the elucidation of questions of the stereochemistry of such tricyclic systems [2], and for the stereospecific synthesis of compounds related to this class of natural substances. For this reason we studied the diene condensation of the diene (I) and its cyclic ketal (IV) with maleic anhydride; some of the results obtained in this way are discussed in the present communication.

The reaction of both dienes with maleic anhydride occurs readily and leads, as in the case of the condensation of quinone, to a mixture of stereo-isomeric adducts, the proportions of which depend on the temperature during the condensation. Thus, the ratio of the adducts (V) and (VI) when the reaction is carried out with the diene (I) at temperatures below 0° is 3.4 : 1, while when the reaction is carried out in boiling benzene solution (2 hrs), the ratio is 2.5 : 1. The condensation of the diene (IV) with maleic anhydride leads to a mixture of the isomers (VII) and (VIII) in a 4 : 1 ratio.

Since both adducts are formed at a low temperature in each case, it is obvious that these pairs of isomers are formed according to the principal of endo-position, and must differ between themselves only in the configuration at the angular methyl group. In analogy with the reaction of the diene (I) and quinone [1], which was studied earlier, there is every reason to consider that the adducts (V) and (VII) which are formed predominantly in the low temperature condensation have the configuration corresponding to the addition of maleic anhydride to the less hindered side opposite the angular methyl group of the diene. Correspondingly, the adducts (VI) and (VIII), isomeric with these,

must have the configuration which follows from the addition of the maleic anhydride to the diene from the side of the methyl group.



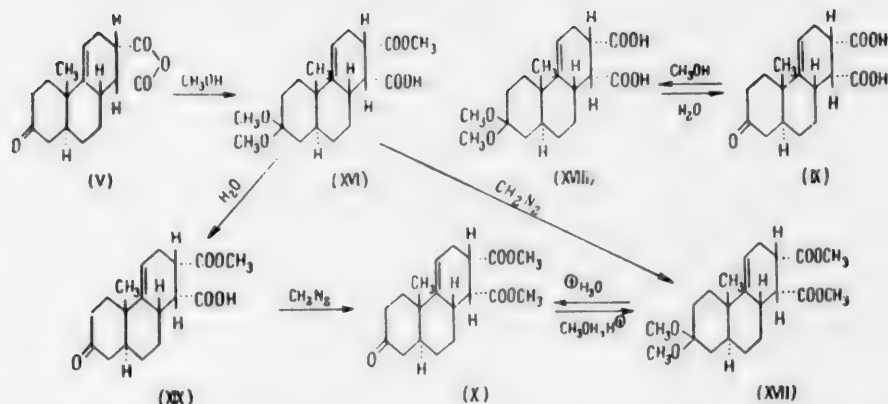
This classification of the adducts (V) and (VII), and correspondingly of the adduct (VI) and (VIII), to one steric series was confirmed by their hydrolysis. Thus, hydrolysis of the keto anhydride (V) with water, and of the ketal anhydride (VII) with 50% acetic acid forms one and the same keto acid (IX), which was characterized as the keto diester (X). Analogously, from the adducts (VI) and (VIII) there is obtained the isomeric keto acid (XI), which gives the corresponding keto diester (XII).

It was observed that hydrolysis of the ketal anhydride (VII) with water or methanol led only to the opening of the anhydride ring, and gave respectively the cyclic ketal acid (XIII) and the half ester (XIV), treatment of which with diazomethane led to the ketal diester (XV). This occurrence was of definite interest, since in this way the functional derivatives of the tricyclic- α -dicarboxylic acid with protected keto groups could be obtained and these are necessary for the realization of the subsequent transformations of the carboxyl groups.

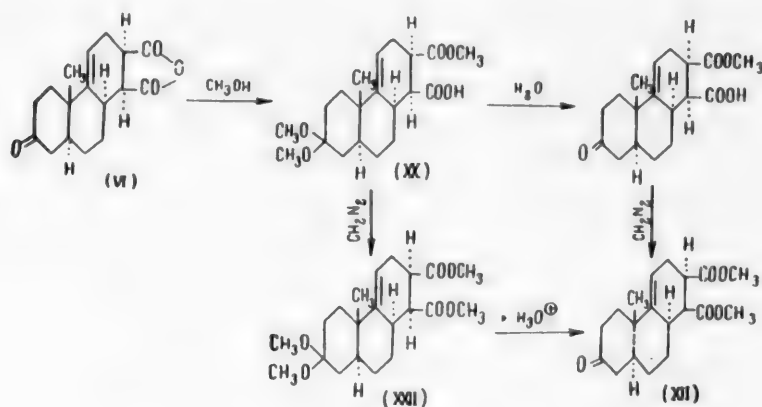
Direct ketalization of the keto group under the influence of the acidity of the carboxyl group of these acids is another method of protecting it; this leads to non-cyclic ketals.

Boiling the keto anhydride (V) with anhydrous methanol gave not the keto half-ester, but the dimethyl ketal half-ester (XVI), which by treatment with diazomethane yielded the dimethyl ketal diester (XVII); this was obtained also by ketalization of the keto diester (X) in the presence of acetic acid.

Similarly, boiling the keto dicarboxylic acid (IX) with methanol yielded the corresponding dimethyl ketal acid (XVIII), which on reaction with diazomethane gave the same dimethyl ketal diester (XVII). The presence of the dimethyl ketal group in all of these compounds was proven by the determination of the quantity of methoxyl groups and by the absence in their infra-red spectra of absorption bands in the 1717-1720 cm^{-1} interval, which is characteristic of the free keto group. The structure of the half-ester (XVI), just as for the other half-esters described in this article, was assumed in analogy with the cases earlier studied [3, 4]; it is shown for these substances that hydrolysis of the anhydride ring with methanol leaves free the more hindered carboxyl group.



As has been shown [5], the formation of a dimethyl ketal can occur when ketones are heated with anhydrous methanol in the presence even of acetic acid; ketals are easily hydrolyzed by water to the original ketone even in weakly acidic media. The fact that in our case ketalization occurs on simple boiling of the keto half-esters and the keto acids in anhydrous methanol shows that this reaction occurs under the influence of the free carboxyl groups of these compounds. Confirmation of this is evident in the capability of the dimethyl ketal half-ester (XVI) and acid (XVIII) to hydrolyze when boiled in a water-acetone solution to form the keto half-ester (XIX) and the corresponding keto acid (IX), while the dimethyl ketal diester (XVII) is unable to undergo this reaction. Hydrolysis of the dimethyl ketal group of this compound occurs only by heating with aqueous acetic acid and gives the keto diester (X) described above. A similar regularity in ketalization and hydrolysis of the dimethyl ketal takes place in the case of the second isomeric anhydride (VI). When it is boiled with methanol the dimethyl ketal half-ester (XX), is obtained, which is unstable, and even during crystallization from aqueous acetone is hydrolyzed to the keto half-ester (XXI); this gives the keto diester (XII) which was described above when it is treated with diazomethane.



In contrast, the dimethyl ketal diester (XXII), which is formed from the dimethyl ketal half-ester (XX) by treatment with diazomethane is a comparatively stable compound, and it is not hydrolyzed by neutral aqueous solutions.

All this data show that the free carboxyl groups in the tri-cyclic-o-dicarboxylic acids described above are sufficiently acidic to cause ketalization of the keto group in anhydrous alcoholic medium, or to cause hydrolysis of the ketal group in the presence of water. However, this acidity, as was shown above, is insufficient to cause hydrolysis of the cyclic ketals (XIII) and (XIV), which are so stable that they do not hydrolyze when boiled in aqueous solution.

EXPERIMENTAL

The condensation of trans-1-vinyl-6-keto-9-methyl- Δ^1 -octalin (I) with maleic anhydride. a) To a solution of 4.4 g of the crystalline diene (I) [6] in 5 ml of benzene was added a solution of 2.27 g of maleic anhydride in

10 ml of benzene; the benzene boiled because of the spontaneous evolution of heat, and a crystalline precipitate was formed. After several hours the crystalline reaction product was filtered off and 3.35 g of the adduct (V) of m.p. 204-206° was obtained; this melted at 212-213° after recrystallization from acetone.

ν (in chloroform): 1717 cm^{-1} (K 1153); 1782 cm^{-1} (K 2350); 1848 cm^{-1} (K 444).*

Found %: C 70.61, 70.85; H 7.14, 7.19. $\text{C}_{17}\text{H}_{20}\text{O}_4$. Calculated %: C 70.81; H 6.99.

The benzene was distilled in vacuo from the mother liquor, ether was added to the residue, and the crystalline product was filtered off. The yield of the crystalline adduct (VI) of melting point 136-139° was 1.65 g; after recrystallization from benzene it had the melting point 148-149°.

ν (in chloroform): 1711 cm^{-1} (K 924); 1788 cm^{-1} (K 1885); 1872 cm^{-1} (K 471).

Found %: C 70.91, 70.78; H 6.99, 6.82. $\text{C}_{17}\text{H}_{20}\text{O}_4$. Calculated %: C 70.81; H 6.99.

b) A solution of 0.52 g of maleic anhydride in 3 ml of benzene was added to a solution of 1 g of the crystalline diene (I) in 1 ml of benzene and the mixture was boiled for 2 hrs. After cooling, the adduct (V), 750 mg, with m.p. 205-208° was filtered off; it was identical to that described above. After removal of the benzene from the mother liquor and the addition of ether there was isolated 470 mg of the adduct (VI) of m.p. 138-142°. By crystallization from benzene there was obtained 320 mg of the adduct (VI) with m.p. 144-145°, identical with that described above.

c) A solution of 0.52 g of maleic anhydride in 3 ml of benzene was added to a solution of 1 g of the crystalline diene (I) in 1 ml of benzene cooled to 0°, and the reaction mixture was let stand at this temperature overnight. The crystalline product which separated was filtered off and identified as the adduct (V) with m.p. 195-200° (950 mg). A single crystallization from acetone gave 820 mg of the adduct (V) of m.p. 204-207°. From the mother liquor after a single crystallization from benzene there was obtained 240 mg of the adduct (VI) of m.p. 144-145°.

The condensation of trans-1-vinyl-6-ethylenedioxy-9-methyl- Δ^1 -octalin (IV) with maleic anhydride. The diene (IV) was obtained by adding a solution of 80 mg of p-toluenesulfonic acid in 5 ml of ethylene glycol to a solution of 2 g of crystalline diene (I) in 40 ml of benzene, and boiling the reaction mixture for 4 hrs with stirring; a water separator was used. After cooling the mixture, the upper layer was separated, washed with a solution of sodium bicarbonate and then with water, and was dried over magnesium sulfate. The trans-1-vinyl-6-ethylenedioxy-9-methyl- Δ^1 -octalin (IV) thus obtained was used for the diene synthesis without further purification. After removal of the greater part of the benzene, 1 g of maleic anhydride in 6 ml of benzene was added to the residue; the mixture became warm and crystals were abundantly formed. After several hours the crystalline product was filtered off, yielding 1.6 g of the adduct (VII) of melting point 203-205°; the substance melts at 207-207.5° and gives a melting point depression with the adduct (V). An additional 0.2 g of the same adduct (VII) was obtained from the mother liquor on standing.

ν (in chloroform): 1780 cm^{-1} (K 2020); 1851 cm^{-1} (K 352).

Found %: C 68.54, 68.47; H 7.11, 7.37. $\text{C}_{19}\text{H}_{24}\text{O}_5$. Calculated %: C 68.65; H 7.28.

Following partial evaporation of the benzene mother liquor and the addition of hexane, there was isolated 0.45 g of crystals with m.p. 135-140°. The adduct (VIII) of m.p. 152-153° was obtained after three crystallizations from a mixture of benzene and petroleum ether.

ν (in chloroform): 1786 cm^{-1} (K 1960); 1869 cm^{-1} (K 360).

Found %: C 68.15, 68.17; H 7.33, 7.45. $\text{C}_{19}\text{H}_{24}\text{O}_5$. Calculated %: C 68.65; H 7.28.

The keto dicarboxylic acid (IX). A mixture of 800 mg of the adduct (V) and 10 ml of 80% aqueous dioxane were boiled for 10 hrs; the solvent was then distilled away in vacuo. This yielded the keto acid, 780 mg, which after reprecipitation from aqueous acetone melted at 200-201°.

Found %: C 66.95, 66.88; H 7.21, 7.28. M 303.8 (by titration with sodium hydroxide). $\text{C}_{17}\text{H}_{22}\text{O}_5$. Calculated %: C 66.65; H 7.24. M 306.3.

* All infra-red spectra for this work were made by T. M. Fadeeva.

b) A solution of 130 mg of the adduct (VII) in 16 ml of 50% acetic acid was boiled for 8 hrs reflux, the solvent was completely removed in vacuo, and the residue was dissolved in acetone. An acid of m.p. 200-201° was isolated after the addition of water; it did not give a depression of the melting point with the substance obtained above.

The keto diester (X). A suspension of 300 mg of the acid (IX) in ether was treated with an ether solution of diazomethane; the solvent was removed in vacuo. The yield of the keto diester was 270 mg, m.p. 130-131° (from aqueous methanol).

ν (in chloroform): 1717 cm^{-1} (K 1750); 1734 cm^{-1} (K 2110).

Found %: C 68.52, 68.51; H 7.61, 7.81. $\text{C}_{19}\text{H}_{26}\text{O}_5$. Calculated %: C 68.24; H 7.84.

The keto dicarboxylic acid (XI). A solution of 160 mg of the adduct (VI) in 2 ml of 80% dioxane was heated for 10 hrs at 50-60°, the solvent was removed in vacuo, and after recrystallization from aqueous dioxane there was obtained 100 mg of the keto acid melting at 258-260° with preliminary softening at 215-218°.

Found %: C 66.36, 66.46; H 7.21, 7.17. $\text{C}_{17}\text{H}_{22}\text{O}_5$. Calculated %: C 66.65; H 7.24.

b) A solution of 100 mg of the adduct (VIII) in 14 ml of 50% acetic acid was boiled for 8 hrs, the solvent was completely removed in vacuo and the residue was dissolved in acetone. The addition of water precipitated an acid, which after recrystallization from aqueous acetone melted at 259-261° with preliminary softening at 220°, and which did not give a melting point depression with the substance obtained above.

The keto diester (XII). A suspension of 50 mg of the acid (XI) in ether was treated with an ether solution of diazomethane and the solvent was removed in vacuo. In this way was obtained 40 mg of the keto diester with m.p. 150-151° (from hexane).

ν (in chloroform): 1736 cm^{-1} (K 1863).

Found %: C 67.85, 68.00; H 7.87, 7.80. $\text{C}_{19}\text{H}_{26}\text{O}_5$. Calculated %: C 68.24; H 7.84.

The ethylene ketal of the dicarboxylic acid (XIII). A solution of 690 mg of the adduct (VII) in 12 ml of 85% aqueous dioxane was boiled for 8 hrs; water was then added until crystallization began. The ketal acid was separated, 590 mg, m.p. 203-204°; after 2 crystallizations from acetone this melted at 219-220°.

Found %: C 65.36, 65.50; H 7.58, 7.52. $\text{C}_{19}\text{H}_{26}\text{O}_6$. Calculated %: C 65.12; H 7.48.

The ethylene ketal half-ester (XIV). A suspension of 400 mg of the adduct (VII) in 7 ml of anhydrous methanol was boiled for 18 hrs (until the starting material completely dissolved). The methanol was removed in vacuo. After 3 crystallizations from aqueous methanol 160 mg of the ketal half-ester was isolated melting at 168-169° with preliminary softening at 160°.

ν (in chloroform): 1728 cm^{-1} (K 1728); 1711 cm^{-1} (K 1260).

Found %: C 65.86, 65.87; H 7.74, 7.82. $\text{C}_{20}\text{H}_{28}\text{O}_6$. Calculated %: C 65.91; H 7.74.

The keto half-ester (XIX) described below can be obtained in good yield by boiling this ethylene ketal with 50% acetic acid.

The ethylene ketal diester (XV). A methanol solution of 0.4 g of the ketal acid (XIII) was treated with an ether solution of diazomethane, the solvent was removed, and the residue was recrystallized from hexane and aqueous methanol. The ethylene ketal diester was obtained, 0.3 g, m.p. 96-97°.

ν (in chloroform): 1734 cm^{-1} (K 2020).

Found %: C 66.98, 67.00; H 7.84, 8.14. $\text{C}_{21}\text{H}_{30}\text{O}_6$. Calculated %: C 66.64; H 7.99.

The same ketal diester was obtained also by treatment of the ketal half-ester (XIV) with diazomethane.

The dimethyl ketal half-ester (XVI). A mixture of 600 mg of the anhydride in 7.5 ml of anhydrous methanol was boiled for 10 hrs and the solvent was removed in vacuo. The half-ester obtained weighed 580 mg and melted at 151-152° (from methanol).

ν (in chloroform): 1734 cm^{-1} (K 1575); 1713 cm^{-1} (K 2160).

Found %: C 65.83, 65.94; H 8.16, 8.09; OCH_3 25.30, 25.46. $\text{C}_{20}\text{H}_{30}\text{O}_6$. Calculated %: C 65.55; H 8.25; OCH_3 26.41.

The dimethyl ketal diester (XVII). a) A solution of 50 mg of the dimethyl ketal half-ester (XVI) in ether was treated with a dry ether solution of diazomethane and the solvent was removed in vacuo. The dimethyl ketal diester obtained weighed 40 mg, and after crystallization from hexane and methanol melted at 94-95°.

ν (in chloroform): 1742 cm^{-1} (K 2610); shoulder at 1715 cm^{-1} .

Found %: C 66.30, 66.46; H 8.31, 8.44. $\text{C}_{21}\text{H}_{32}\text{O}_6$. Calculated %: C 66.30; H 8.48.

b) A solution of 200 mg of the keto diester (X) in 10 ml of anhydrous methanol was boiled for 8 hrs after the addition of 2 drops of acetic acid. After cooling and neutralizing the solution with dry sodium bicarbonate the solvent was evaporated in vacuo; 100 mg of the dimethyl ketal diester (XVII) described above was obtained by the addition of 1 ml of methanol; the substance melted at 94-95° and did not give a melting point depression with the preceding material. This dimethyl ketal diester was stable when boiled in aqueous methanol and could be quantitatively hydrolyzed to the original keto diester (X) only when boiled with aqueous acetic acid.

The dimethyl ketal of the dicarboxylic acid (XVIII). A solution of 200 mg of the keto acid (IX) in 3 ml of anhydrous methanol was boiled for 16 hrs; the solvent was evaporated in vacuo and 180 mg of the dimethyl ketal acid, m.p. 142-143°, was obtained by crystallization of the residue from ether.

ν (in chloroform): 1713 cm^{-1} (K 3420).

Found %: C 64.51, 64.33; H 7.87, 8.05; OCH_3 17.17, 17.30. $\text{C}_{19}\text{H}_{28}\text{O}_6$. Calculated %: C 64.75; H 8.01; OCH_3 18.03.

When boiled with water this dimethyl ketal was quantitatively hydrolyzed to the original keto acid (IX), while by treatment with diazomethane the dimethyl ketal diester (XVII), m.p. 94-95°, described above was obtained.

The keto half-ester (XIX). The keto half-ester, m.p. 173.5-174.5°, was quantitatively obtained by crystallization of 100 mg of the dimethyl ketal half-ester (XVI) from aqueous acetone.

ν (in chloroform): 1738 cm^{-1} (K 1420); 1719 cm^{-1} (K 1824); shoulder at 1705 cm^{-1} .

Found %: C 67.25, 67.73; H 7.50, 7.54. $\text{C}_{18}\text{H}_{24}\text{O}_5$. Calculated %: C 67.48; H 7.55.

By prolonged boiling of this keto half-ester with anhydrous methanol the original dimethyl ketal (XVI) is formed, and by treatment with diazomethane the keto diester (X) described above.

The dimethyl ketal half-ester (XX). A solution of 1 g of the isomeric anhydride (VI) in 20 ml of anhydrous methanol was boiled for 9 hrs. The methanol was partially evaporated, and the crystalline product which separated was filtered off. A substance of melting point 149-150° was obtained, 460 mg, and from this by two crystallizations from methanol the dimethyl ketal half-ester of m.p. 156-157° was isolated.

ν (in chloroform): 1734 cm^{-1} (K 1380); 1713 cm^{-1} (K 1600).

Found %: C 65.92; H 8.20. $\text{C}_{20}\text{H}_{30}\text{O}_6$. Calculated %: C 65.55; H 8.25.

The keto half-ester (XXI). Crystallization of the dimethyl ketal half-ester (XX) from aqueous acetone caused quantitative hydrolysis of the ketal group resulting in the formation of the keto half-ester of m.p. 193-194°.

ν (in chloroform): 1738 cm^{-1} (K 1293); 1719 cm^{-1} (K 1710); 1710 cm^{-1} (K 1710).

Found %: C 67.55, 67.29; H 7.41, 7.48. $\text{C}_{18}\text{H}_{24}\text{O}_5$. Calculated %: C 67.48; H 7.55.

The keto diester (XII) was obtained by treatment of the keto half-ester with diazomethane and recrystallization from hexane and aqueous acetone, it did not give a melting point depression with the other sample.

The dimethyl ketal diester (XXII). A solution of the dimethyl ketal half-ester (XX) in anhydrous methanol was treated with an ether solution of diazomethane which had been dried over potassium hydroxide pellets. After removal of the solvent the product was extracted with hexane. The dimethyl ketal diester melted at 105-105.5° after 2 crystallizations from aqueous acetone.

ν (in chloroform): 1736 cm^{-1} (K 1675); shoulder at 1719 cm^{-1} (K 1336).

Found %: C 66.65; H 8.50. $\text{C}_{21}\text{H}_{32}\text{O}_6$. Calculated %: C 66.30; H 8.48.

This dimethyl ketal did not hydrolyze in water, and it could be transformed into the keto diester (XII) only by boiling with aqueous acetic acid.

SUMMARY

1. The diene condensations of trans-1-vinyl-6-keto-9-methyl- Δ^1 -octalin and its ethylene ketal with maleic anhydride were studied; the reaction led in each case to the formation of two isomeric adducts; their possible configurations are discussed.

2. A dependence of the relative yield of the isomers on the temperature during the condensation was observed; some transformations of these isomers were studied.

3. The easy ketalization of the tricyclic keto acids and half-esters when boiled with methanol was observed; its relation to the acidity of the free carboxyl groups in the molecule is mentioned.

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DERIVATIVES OF INDOLE

XII. THE SYNTHESIS OF 1-(D-β-GLUCOPYRANOSYL)-INDOLE*

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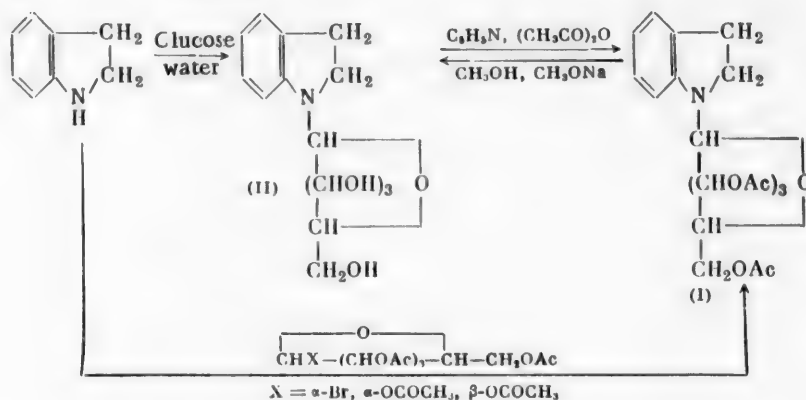
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The synthesis and study of the properties of 1-glycosylindoles is of special interest. One might expect that these substances, constructed analogously to the nucleosides, will possess interesting biological activities. It is known that derivatives of indole play a substantial role in the pathogenesis of leukosis [2]; cases are described where myeloid leukemia has appeared in mice on long exposure to indoles [3]. In the light of these facts a broad investigation of the biological activity of 1-glycosylindoles acquires a special interest.

Not a single representative of this new class of compound has been synthesized previously. For the preparation of 1-(D-glycosyl)-indole in our work we made use of the method worked out by A. P. Terent'ev and M. N. Preobrazhenskaya [4] for the introduction of substituents into the indole nucleus. In our case we obtained 1-(tetraacetylglucosyl)-indole by the dehydrogenation of 1-(tetraacetylglucosyl)-indoline; deacetylation of the former led to 1-(glucosyl)-indole.

Thus, 1-(D-β-tetraacetylglucopyranosyl)-indoline (I), which is an acylated arylaminoglycoside, was obtained in one step.



To obtain the substance (I), methods were utilized ordinarily applied to the synthesis of acylated arylaminoglycosides [5]. Heating a mixture of indoline and glucose with a small quantity of water gave 1-(D-glucosyl)-indoline (II) in amorphous form. (The material was not further purified); acetylation gave (I). It has been shown previously [5, 6] that acetylated arylaminoglycosides ordinarily give mixtures of α - and β -anomers. We undertook fractional crystallization of the acetylated product (II) in alcohol, measuring the specific rotation of each fraction. It was shown that only one isomer is formed and that no other substance possessing a higher positive or negative specific rotation is present. Only one definite spot was obtained by chromatographing the indoline (I) on paper.

Thus the acetylation of the indoline (II) gives only one anomer: 1-(D-tetraacetylglucosyl)-indoline (I).

* Preliminary communication [1].

The same anomer (I) was obtained from indoline and β -pentaacetylglucose in 77.5% yield; a 56% yield of 1-acetylindoline was also isolated. In this case also it was shown by the method of fractional crystallization with the determination of the specific rotations of the fractions that no noticeable quantity of a second anomer is formed. An 87% yield of (I) and a 98% yield of 1-acetylindoline were obtained from α -pentaacetylglucose and indoline. α -Acetobromoglucose and indoline give (I) in 57% yield.

It is most convenient to obtain (I) from indoline and β -pentaacetylglucose.

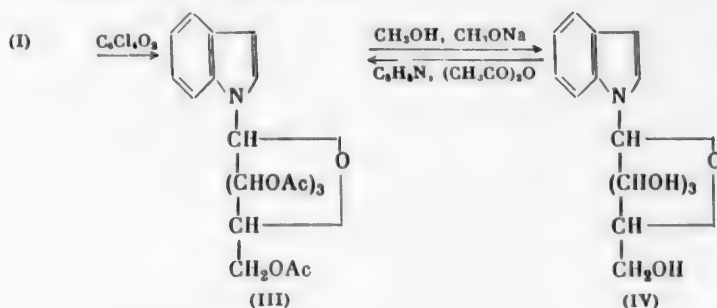
The fact that both α - and β -derivatives of glucose give one and the same anomer can be explained only by assuming that this anomer has the β -configuration. It is known [7] that in reactions of nucleophilic substitution, α -bromoglucosides as a rule form β -glucosides (trans-position of the substituents at C_1 and C_2). According to the accepted mechanism of nucleophilic substitutions in the glucoside series [7, 8], this β -(trans)-anomer must predominate in the formation of the glucoside from α - and β -pentaacetylglucoses. The β -configuration of the substance (I) is also confirmed by the magnitude of its specific rotation.

A study of Brigleb models showed that the indoline is in an equatorial position in the β -anomer (I); the structure of the α -anomer is apparently less advantageous, since the indoline in the α -anomer occupies an axial position.

Apparently the absence of mutarotation of aqueous solutions of (II) may also be explained by the influence of this factor. Analytically pure 1-(D- β -glucopyranosyl)-indoline (II) was obtained by deacetylation of (I) [9]. The amorphous, hygroscopic substance was stable for several weeks and did not show mutarotation in water or in formamide.

Hydrolysis of (I) with dilute acetic acid gave indoline and 2,3,4,6-tetraacetylglucopyranose which was isolated as α -pentaacetylglucopyranose.

1-(D- β -Tetraacetylglucopyranosyl)-indole (III) was obtained by the dehydrogenation of (I) with chloranil in dry boiling xylene (traces of water caused tar formation).



It is interesting that the compound (III) could be isolated in two crystalline modifications – one labile, the other stable. By slow heating or by standing in sunlight the labile form was converted to the stable. The infra-red spectra of both forms were identical (Nujol mull).

Paper chromatography was used to follow the process of dehydrogenation. Ehrlich's reagent colors (I) a bright yellow and (III) a bright pink. The ultra-violet absorption spectrum of (I) is similar to the ultra-violet spectra of other derivatives of indoline [10], but (III) possesses an ultra-violet absorption spectrum characteristic of indole (Fig. 1). The deacetylation of (III) [9] gave a quantitative yield of 1-(D- β -glucopyranosyl)-indole. This substance is stable, amorphous, and extremely hygroscopic. Solutions in water and formamide do not mutarotate. The pyranose structure was confirmed by acetylation with acetic anhydride in pyridine which gave a quantitative yield of 1-(D- β -tetraacetylglucopyranosyl)-indole (III).

The ultra-violet absorption curve of 1-(D- β -glucopyranosyl)-indole (IV) has the form characteristic of indole compounds, while the compound (II) has an ultra-violet spectrum characteristic of indolines (Fig. 2). Ehrlich's reagent colors (IV) a bright pink and (II) a bright yellow. The R_f values for (II) and (IV) are very close.

The structure of 1-(D- β -glucopyranosyl)-indole was also confirmed by calculation of the molecular rotation. According to Hudson [11], the molecular rotation (M) is equal to the sum of the rotations of the glucoside atom (A)

and the rotation of the remaining parts of the molecule (B). For the β -anomer, M_β is equal to $[\alpha]_D^{20} \times$ the molecular weight = $-A + B$.

The values of B for derivatives of tetraacetylglucopyranose is known to be 20500 (in chloroform or in anhydrous alcohol) [12]. In different solvents B varies within the limits 18500-22000. According to the data of the literature [6], one can calculate the value of B for α - and β -tetraacetylglucopyranosyl-anilines as $B = \frac{M_\alpha + M_\beta}{2}$ (chloroform).

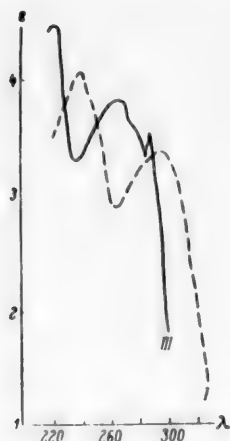


Fig. 1. The ultraviolet absorption spectra of 1-(D- β -tetraacetylglucopyranosyl)-indoline (I) and 1-(D- β -tetraacetylglucopyranosyl)-indole (III).

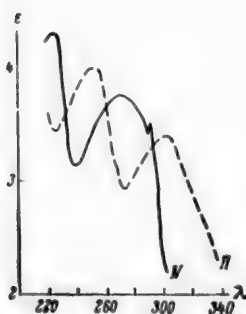


Fig. 2. The ultraviolet absorption spectra of 1-(D- β -glucopyranosyl)-indoline (II) and 1-(D- β -glucopyranosyl)-indole (IV).

The values of A for (I) or (III) can be calculated from the known values of B. In chloroform for (I): $+11.3 \cdot 449.5 = -A + B = -A + 20500$, $A = 15431$. The contribution of the glucoside atom of 1-glycosylindolines is +15431. For (III) in chloroform: $+1.5 \cdot 447.5 = -A + B = -A + 20500$, $A = 19839$. The contribution of the glucoside atom of 1-glycosylindoles is +19839.

One can determine the value of B from the value of A for the deacetylated glucosides (I) and (IV); this value of B must coincide with the value of B found in the literature for derivatives of glucopyranose. The calculations are to a certain degree approximate, since the values of A are calculated for chloroform, while the specific rotations of (I) and (IV) were measured in water and formamide. But as has already been pointed out the magnitudes of A and B are not changed significantly when the solvent is changed.

For (II) (in water): $M_\beta = -15 \cdot 281.3 = -A + B = -15431 + B$, $B = 11211$.

For (II) (in formamide): $M_\beta = 8.5 \cdot 281.3 = -15431 + B$, $B = 13040$.

For (IV) (in water): $M_\beta = -23 \cdot 279.3 = -A + B = -19839 + B$, $B = 13415$.

For (IV) (in formamide): $M_\beta = -20 \cdot 279.3 = -19839 + B$, $B = 14253$.

The value of B calculated from the data for glucose is 11800 for derivatives of glucopyranose, varies from 10,000 to 12,000 for alkylglucopyranisides, and for phenylglucopyranisides $B = 15,700$. For glucofuranoside $B = 2500$ [11]. Hence, the calculation according to Hudson [11] confirms the glucopyraniside structure of both (II) and (IV).

EXPERIMENTAL

1-(D- β -tetraacetylglucopyranosyl)-indoline (I). a) A mixture of 6 g of freshly distilled indoline, 1 ml of water, and 9 g of glucose were heated and stirred on a boiling water bath. After 15 min the solution became transparent; the heating was continued for an additional 30 min, and the solution was then cooled and diluted with 20 ml of methyl alcohol. The precipitate was filtered off. A substance, 0.2 g, was obtained, the structure of which has not been established. The mother liquor was evaporated in vacuo on a water bath; the residue was washed with 300 ml of ether, and then was dried in a vacuum desiccator over P_2O_5 . The substance foamed in the vacuum, and on standing over P_2O_5 solidified. The amorphous powder was dissolved in 80 ml of absolute pyridine; the solution was cooled to 0° and stirred while 35 ml of acetic anhydride was added drop-wise. After 12 hrs the reaction mixture was poured over ice (1 kg); an oil precipitated which began to crystallize after several hours of stirring. The crude substance weighed 15.8 g; after 4 recrystallizations from alcohol the yield of (I) was 12.93 g (57.2%).

M.p. 117.8-118.5° $[\alpha]_D^{20} + 5.5^\circ$ (CCl_4 , c 4), $[\alpha]_D^{20} + 11.7^\circ$ (benzene, c 6); $[\alpha]_D^{20} + 9.7^\circ$ (dioxane, c 6); $[\alpha]_D^{20} + 11.3^\circ$ ($CHCl_3$, c 6).

Found %: C 58.91; H 6.10; N 3.33; CH_3CO 38.2. $C_{22}H_{27}O_9N$. Calculated %: C 58.79; H 6.05; N 3.12; CH_3CO 38.3.

b) A mixture of 5 g of β -pentaacetylglucose, 5 g of indoline, and 5 ml of acetic acid was dissolved in 100 ml of alcohol and allowed to stand overnight. Crystals of (I) were formed; these were filtered off after the solution was cooled. The yield of crude (I) was 5.26 g. After 2 crystallizations from alcohol, 4.48 g (77.5%) of (I) with m.p. 117-118° was obtained. By dilution of the mother liquor with water, 2.3 g of a substance was isolated which yielded 1.15 g (56%) of 1-acetyl-indoline, m.p. 100-101.5°, after several recrystallizations from aqueous alcohol. A test mixture with a known sample of 1-acetylindoline did not give a melting point depression.

Analogously, from 1 g of α -pentaacetylglucose and 1 g of indoline there were obtained 1 g (87%) of (I), m.p. 117.5-118°, and 0.4 g (98%) of 1-acetylindoline, m.p. 98-100.5°.

c) A solution of 3.7 g of α -acetobromoglucose and 3.3 g of indoline in 50 ml of dry benzene was heated for half an hour on a boiling water bath and then let stand overnight. The precipitated crystals of indoline hydrobromide were filtered off (0.62 g, 34%); the benzene solution was evaporated in vacuo and the residue was recrystallized from alcohol. The yield of (I) was 2.3 g (57%), m.p. 115-116.5° and $[\alpha]_D^{20} + 11.7^\circ$ (benzene).

The hydrolysis of 1-(D- β -tetraacetylglucopyranosyl)-indoline (I). A mixture of 100 ml of 30% acetic acid, 30 ml of alcohol, and 4.5 g of (I) was steam distilled. Three liters of distillate were collected. The distillate was made basic with sodium carbonate and extracted with ether; the ether solution was dried with potash and added to an ether solution of picric acid. The yield of indoline picrate was 2.9 g (83.5%). The melting point was 164-166° (dec.) (from alcohol). The melting point of a known sample of indoline picrate was 164-165° (dec.)—of the mixture 164-165° (dec.).

The residue from the steam distillation was evaporated to dryness in vacuo and the viscous oil so obtained was heated for 20 min on a boiling water bath with 50 ml of acetic anhydride and 1 g of anhydrous zinc chloride. The mixture was poured into water and after 2 hrs it was extracted with chloroform; the dark solution was dried over magnesium sulfate. After removal of the chloroform in vacuo an oil remained which rapidly began to crystallize. After recrystallization from alcohol the colorless crystals weighed 0.9 g, m.p. 110-110.5° and $[\alpha]_D^{20} + 72^\circ$ (benzene, c 4.7). The substance gave no depression of the melting point with a known sample of α -pentaacetylglucose. An additional 1 g of α -pentaacetylglucose was isolated from the mother liquor (the total yield was 49%).

1-(D- β -tetraacetylglucopyranosyl)-indole (III). (I), 4.5 g, and chloranil, 2.5 g, were dissolved in 150 ml of dry m-xylene and 40 ml of the solvent was distilled away (b.p. 138°). The solution which contained no trace of moisture was boiled for 6 hrs under reflux; it was protected from atmospheric moisture by a tube of calcium chloride. Another 70 ml of xylene was distilled off and the residue was placed for several hours in a refrigerator. The precipitated crystals were filtered off, washed on the filter with cold alcohol, and recrystallized from alcohol. The yield of crude (III) was 1.4 g. The mother solution was passed through a chromatographic column containing 40 g of aluminum oxide. The first 50 ml of effluent xylene were colored yellow and contained 0.1 g of chloranil; after that (III) was washed out with more xylene. The dark solution (about 200 ml) was evaporated to dryness and the residue was recrystallized from alcohol. An additional 0.5 g of crude (III) was obtained. All of the crude (III) was recrystallized several times from alcohol, using activated charcoal. The yield of 1-(D- β -tetraacetylglucopyranosyl)-indole was 1.45 g (32%).

M.p. 148.5-149° (from alcohol); 157.8-158.2° (from petroleum ether). $[\alpha]_D^{20} + 1.5$ (CHCl₃, c 5.5).

Found %: C 59.05; H 5.86; N 3.05; CH₃CO 38.4. C₂₂H₂₅O₉N. Calculated %: C 59.05; H 5.63; N 3.13; CH₃CO 38.5.

The paper chromatography of 1-(D- β -tetraacetylglucopyranosyl)-indoline (I) and 1-(D- β -tetraacetylglucopyranosyl)-indole (III). "Whatman's" paper (Leningrad) was used for the chromatography of (I) and (III). The starting spots of (I) and (III) contained 60 γ . The paper was dampened with a 50% mixture of formamide and acetone; it was pressed between two pieces of filter paper, dried for 10 min in air at 25°, and placed in a chamber with isooctane.

Only chemically pure formamide with a pH of 8 is suitable for the impregnation. The chromatogram was dried in air and then heated in a cabinet at 100° for 10 min. For development the paper was moistened with a 1% solution of p-dimethylaminobenzaldehyde in a mixture of alcohol (98 ml) and hydrochloric acid (2 ml). Yellow spots of (I) immediately appeared. It was then moistened with a 2% solution of p-dimethylaminobenzaldehyde in a 50% mixture of alcohol and hydrochloric acid. The pink spots of (III) immediately appeared. It was then moistened with a 2% solution of p-dimethylaminobenzaldehyde in a 50% mixture of alcohol and hydrochloric acid. The pink spots of (III) immediately appeared. (III) remained at the starting spot; the R_f of (I) = 0.15.

It is less convenient to chromatograph in heptane on paper impregnated with β -phenoxyethanol. (III) remained at the starting point; the R_f of (I) = 0.04.

1-(D- β -glucopyranosyl)-indoline (II). To a suspension of 3.7 g of (I) in 50 ml of anhydrous methyl alcohol was added 1 ml of 0.1 N solution of sodium methylate and the mixture was stirred at room temperature. After 5 min the solid was completely dissolved. The mixture was stirred for another 15 min, 15 ml of water was added, and a stream of carbon dioxide was passed into the reaction mixture for 1 hr. The solution was evaporated in vacuo on a water bath to dryness and the residue was dried for 24 hrs in a vacuum desiccator over P_2O_5 . The amorphous substance which remained was dissolved in a mixture of anhydrous methyl alcohol (20 ml) and absolute ether (5 ml); the solution was cooled and a current of carbon dioxide was passed in for 15 min. The solution of the glucoside was filtered from the sodium bicarbonate and was then evaporated to dryness in vacuo on a water bath. The foamy material which remained was washed with dry ether and was then dried over P_2O_5 at 78°. (II) was obtained in the form of a colorless, amorphous, hygroscopic, solidified foam. The yield was 2.3 g (quantitative). The substance gradually softened at about 30°; the melt became transparent about 100-110°. $[\alpha]_D^{20}$ -15° (water, c 4.4); $[\alpha]_D^{20}$ -8.5° (formamide, c 2.7).

Found %: C 59.25; H 7.15; N 4.97. $C_{14}H_{19}O_5N$. Calculated %: C 58.81; H 6.83; N 4.98.

R_f = 0.82 in the system butanol-pyridine-water (3 : 1 : 1.5) (upper layer). Developed as for (I). A yellow spot.

1-(D- β -glucopyranosyl)-indole (IV). The deacetylation of (III) and the isolation of (IV) was carried out in the same manner as described for (I) and (II). From 3 g of (III) there was obtained 1.85 g of (IV) (quantitative yield) in the form of a colorless, friable, amorphous mass (a solidified foam). The substance is very hygroscopic. At a temperature of about 80° it becomes resinous; toward 100° the melt becomes transparent. $[\alpha]_D^{20}$ -23° (water, c 5.8); $[\alpha]_D^{20}$ -20° (formamide, c 1).

Found %: C 58.70; H 6.51; N 4.97; H_2O 1.10. $C_{14}H_{17}O_5N \cdot 2H_2O$. Calculated %: C 59.43; H 6.19; N 4.95; H_2O 1.27.

R_f = 0.89 in the system butanolpyridine-water (3 : 1 : 1.5) (upper layer). Development as for (III). A pink spot.

SUMMARY

1. A method of synthesizing 1-(glycosyl)-indoles from acetylated 1-(glucosyl)-indolines by means of dehydrogenation and subsequent deacetylation is presented.
2. 1-(D- β -glucopyranosyl)-indole and 1-(D- β -glucopyranosyl)-indoline were prepared.
3. The presence of the pyranose ring in the molecules of 1-(D- β -glucopyranosyl)-indole and 1-(D- β -glucopyranosyl)-indoline was shown by calculating the molecular rotation according to Hudson.
4. Conditions were found for chromatographing on paper the compounds: glucosyl-indole, glucosyl-indoline, and their acetyl derivatives.

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THE SYNTHESIS OF THIOPHENE ANALOGS OF DI- AND TRIMETHOXYCHALCONES AND THEIR VINYLOGS

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The first thiophene analog of chalcone was obtained by the condensation of acetothienone and benzaldehyde in the presence of hydrogen chloride [1]. Grishkevich-Trokhimovskii, and Matsurevich [2] have described the crotonic condensation of the 2-thiophenaldehyde with acetone, acetophenone, and other carbonyl compounds in the presence of a 20% solution of sodium methylate or of a 10% solution of sodium hydroxide. These were the initial syntheses of α, β -unsaturated ketones containing the thiophene ring.

However, the literature since that time contains little information on such compounds. An article [3] was published which described the synthesis and polymorphism of thiophene and furan analogs of chalcones. In the last decade there has been a noticeable increase of interest in α, β -unsaturated ketones of the heterocyclic series, especially derivatives of thiophene. Thus, reports have appeared on the study of their absorption spectra [4], on the search for biologically active preparations among them [5], on their usefulness as intermediates in organic syntheses [6], etc. [7].

A considerable number of the thiophene analogs of chalcone and their vinylogs which contain pentadienones having one or two heterocyclic nuclei are known at the present time. Thus, for example, we [8] recently described a series of 1-thienyl-3-phenylpropenones and 1-thienyl-5-phenylpentadienones which contained a single nitro or methoxy group in the aromatic nucleus, as well as some other unsaturated thiophene ketones.

In the present work we set ourselves the goal of obtaining a systematic series of propenones and pentadienones containing thiophene and aromatic rings in the 1,3- and 1,5-positions—the aromatic substituents being the 2,4-dimethoxyphenyl and 2,4,6-trimethoxyphenyl radicals so that they would have a strong electropositive character.

The syntheses of the di- and trimethoxy derivatives were accomplished through the crotonic condensation of 2-thiophenaldehyde, 2-thiophenacetaldehyde, and 2-acetothienone with 2,4-dimethoxy- and 2,4,6-trimethoxy-acetophenone, benzaldehyde, cinnamaldehyde, and benzalacetone according to the scheme



R and R₁ = the thienyl and aryl radicals.

In spite of the data in the literature which indicate that electropositive substituents in the aromatic nucleus hinder the crotonic condensation [9], the reaction proceeded easily in all cases at room temperature in aqueous alcoholic solution in the presence of a small quantity of sodium hydroxide, and was usually finished within a few hours.

The majority of the intermediates necessary for these condensations were obtained by methods described in the literature, only 2,4-dimethoxycinnamaldehyde, 2,4-dimethoxy- and 2,4,6-trimethoxybenzalacetone were synthesized by original methods. The synthesis of 2,4-dimethoxycinnamaldehyde from a compound not ordinarily available is described in the literature [10]. We were able to obtain it easily by the ordinary crotonic condensation from 2,4-dimethoxybenzaldehyde and acetaldehyde. It is interesting that an attempt to obtain the analogous compound 2,4,6-trimethoxycinnamaldehyde in the same fashion was unsuccessful.

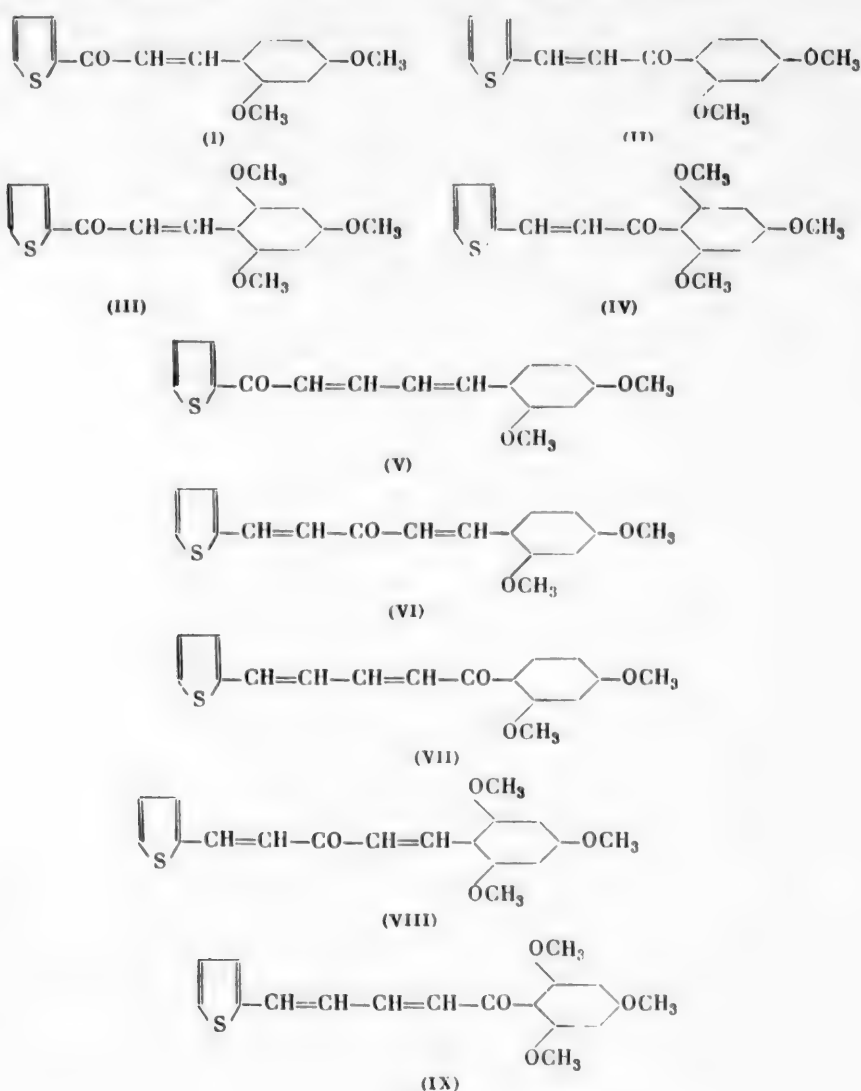
2,4-Dimethoxybenzalacetone was obtained by Berlin and Sycheva [11] from 2,4-dimethoxybenzaldehyde and acetone in the form of an oil, and by Nesmeyanov, Kochetkov, and Matov through the chlorovinyl ketone in 14% yield with a melting point of 62°. We obtained this product easily in about 80% yield in pure form with a melting point of 64-65° through the reaction of 2,4-dimethoxybenzaldehyde with a large excess of acetone. The use of a large excess of acetone for this synthesis is necessary since a side reaction may occur through the interaction of two

molecules of the corresponding aldehyde with one molecule of acetone, leading to the formation of the more difficultly soluble derivative of dibenzalacetone, which contaminates the main product and lowers its yield. We obtained 2,4,6-trimethoxybenzalacetone analogously; it had been obtained earlier, although in impure form [13].

The unsaturated ketones (VI) and (VIII) (Table 1) were obtained by two methods, which once again confirmed the structure of these compounds.

All of the thiophene analogs of 2,4-di- and 2,4,6-trimethoxychalcones and their vinylogs – the corresponding pentadienones – were solid, well-crystallized substances, which possessed brilliant halochromic properties. All of them were quite soluble in alcohol, ether, benzene, and numerous other organic solvents, and were insoluble in water.

We synthesized nine thiophene analogs of the di- and trimethoxychalcones and their vinylogs: 1-thienyl-3-(2,4-dimethoxyphenyl)-propenone-1 (I), 1-thienyl-3-(2,4-dimethoxyphenyl)-propenone-3 (II), 1-thienyl-3-(2,4,6-trimethoxyphenyl)-propenone-1 (III), 1-thienyl-3-(2,4,6-trimethoxyphenyl)-propenone-3 (IV), 1-thienyl-5-(2,4-dimethoxyphenyl)-pentadiene-2,4-one-1 (V), 1-thienyl-5-(2,4-dimethoxyphenyl)-pentadiene-1,4-one-3 (VI), 1-thienyl-5-(2,4-dimethoxyphenyl)-pentadiene-1,3-one-5 (VII), 1-thienyl-5-(2,4,6-trimethoxyphenyl)-pentadiene-1,4-one-3 (VIII), 1-thienyl-5-(2,4,6-trimethoxyphenyl)-pentadiene-1,3-one-5 (IX).



The basic data on these products are cited in Table 1, the analyses in Table 2.

TABLE 1. Thiophene Analogs of Chalcone and Their Vinylogs

Ketone	Starting material	Melting point	Yield (in %)	Appearance and color of the ketone	2,4-Dinitrophenylhydrazones	
					appearance	melting point
(I)	2-Acetotheinone and 2,4-dimethoxybenzaldehyde	94°	77	Greenish-yellow, long prisms	Orange-red, fine crystals	210° (Benzene)
(II)	2-Thiophenylaldehyde and 2,4-dimethoxyacetophenone [15]	86.5	73	Greenish-yellow, long slim prisms	Light-red platelets	200 (Benzene)
(III)	2-Acetotheinone and 2,4,6-trimethoxybenzaldehyde [16]	109	95	Greenish-yellow needles	Orange-red needles	232 (Acetic acid)
(IV)	2-Thiophenylaldehyde and 2,4,6-trimethoxyacetophenone [16]	104	84	Greenish-yellow prisms	Dark-red platelets	226 (Acetic acid)
(V)	2-Acetotheinone and 2,4-dimethoxycinnamaldehyde	145	83	Yellow platelets	Red platelets	200 (Benzene)
(VI)	1) 2-Thiophenylaldehyde and 2,4-dimethoxybenzalacetone 2) Thiophenylidenacetone [2] and 2,4-dimethoxybenzaldehyde	71	1) 80 2) 69	Yellow prisms	Reddish-brown, fine crystals	170 (Benzene)
(VII)	2-Thiophenylaldehyde [17] and 2,4-dimethoxyacetophenone	118	78	Yellow needles	Light-red needles	205 (Benzene)
(VIII)	1) 2-Thiophenylaldehyde and 2,4,6-trimethoxybenzalacetone 2) Thiophenylidenacetone and 2,4,6-trimethoxybenzaldehyde	160	1) 83 2) 85	Yellow prisms	Reddish-brown needles	235 (Acetic acid)
(IX)	2-Thiophenylaldehyde and 2,4,6-trimethoxyacetophenone	110	79	Yellow prisms	Red needles	238 (Acetic acid)

EXPERIMENTAL

2,4-Dimethoxycinnamaldehyde. To a solution of 10 g of 2,4-dimethoxybenzaldehyde [14] in 140 ml of methyl alcohol there was added 3 ml of freshly distilled acetaldehyde, 20 ml of a 5% solution of sodium hydroxide, and 40 ml of water. The mixture was mechanically shaken for 7 days. Daily, for the first five days there was added to the mixture 3 ml of acetaldehyde, in all 15 ml. After 7 days, the methyl alcohol was distilled away; the residue was extracted with benzene; the benzene layer was dried over magnesium sulfate. The solvent was distilled off, and the residue was fractionated in vacuo, the fraction distilling at 185-200° (1-2 mm), being collected. A 77% yield (10 g) of almost colorless needles was obtained with m.p. 100° (from petroleum ether and 70% aqueous methanol); this is in agreement with the data of the literature [10].

The 2,4-dinitrophenylhydrazone was obtained in the form of orange-red, fine crystals with m.p. 250° (from benzene).

Found %: N 15.22, 15.32. $C_{17}H_{15}O_6N_4$. Calculated %: 15.04.

The semicarbazone was obtained in the form of yellowish platelets with m.p. 200°, which is in agreement with the data of the literature [10].

TABLE 2. Data of the Elementary Analyses

Ketone	Minimal formula of the ketone	% S		Minimal formula of the 2,4-dinitrophenylhydrazone	% N	
		calc.	found		calc.	found
(I)	$C_{15}H_{14}O_3S$	11.68	11.58, 11.54	$C_{21}H_{18}O_6N_4S$	12.32	12.04, 12.00
(II)	$C_{15}H_{14}O_3S$	11.68	11.67, 11.58	$C_{21}H_{18}O_6N_4S$	12.32	12.19, 12.25
(III)	$C_{16}H_{16}O_4S$	10.53	10.20, 10.66	$C_{22}H_{20}O_7N_4S$	11.55	11.39, 11.71
(IV)	$C_{16}H_{16}O_4S$	10.53	10.20, 10.22	$C_{22}H_{20}O_7N_4S$	11.55	11.39, 11.57
(V)	$C_{17}H_{16}O_5S$	10.67	10.33, 10.75	$C_{23}H_{20}O_8N_4S$	11.65	11.90, 11.94
(VI)	$C_{17}H_{16}O_5S$	10.67	10.31, 10.47	$C_{23}H_{20}O_8N_4S$	11.65	11.74, 11.93
(VII)	$C_{17}H_{16}O_5S$	10.67	10.32, 10.69	$C_{23}H_{20}O_8N_4S$	11.65	11.53, 11.62
(VIII)	$C_{18}H_{18}O_4S$	9.70	9.75, 10.04	$C_{24}H_{22}O_7N_4S$	10.97	11.21, 11.18
(IX)	$C_{18}H_{18}O_4S$	9.70	9.38, 9.40	$C_{24}H_{22}O_7N_4S$	10.97	10.96, 11.16

2,4-Dimethoxybenzalacetone. To a solution of 2 g of 2,4-dimethoxybenzaldehyde in 30 ml of acetone was added 100 ml of water, 30 ml of isopropyl alcohol, and drop-wise and with stirring 10 ml of a 10% solution of sodium hydroxide. On the following day the light yellow crystals which had precipitated were washed with water, and dried in vacuo. The yield was 2 g of colorless platelets, m.p. 64-65° (from petroleum ether and 70% methanol).

Found %: C 69.74, 70.09; H 6.96, 7.16. $C_{12}H_{14}O_3$. Calculated %: C 69.86; H 6.84.

The 2,4-dinitrophenylhydrazone was obtained in the form of dark-red needles, soluble in benzene, chloroform, and acetic acid, and insoluble in water, alcohol, and ether. The melting point was 247° (from benzene).

Found %: N 14.47, 14.61. $C_{18}H_{16}O_6N_4$. Calculated %: N 14.49.

The semicarbazone was isolated as light-yellow platelets of m.p. 206° (from alcohol).

Found %: N 15.89, 16.07. $C_{13}H_{17}O_3N_3$. Calculated %: N 15.95.

The thiosemicarbazone was isolated in the form of yellow needles of m.p. 170°, in agreement with the data of the literature [11].

2,4,6-Trimethoxybenzalacetone was obtained in a manner analogous to the preceding. The colorless needles melted at 123°.

Found %: C 65.94, 65.83; H 7.01, 6.95. $C_{13}H_{16}O_4$. Calculated %: C 66.08; H 6.82.

The 2,4-dinitrophenylhydrazone was isolated in the form of orange-red crystals of melting point 260° (from benzene).

Found %: N 13.58, 13.76. $C_{19}H_{20}O_7N_4$. Calculated %: N 13.45.

The semicarbazone was isolated in the form of greenish-yellow needles of m.p. 182° (from alcohol).

Found %: N 14.48, 14.52. $C_{14}H_{19}O_4N_3$. Calculated %: N 14.31.

The thiosemicarbazone was isolated in the form of yellow, small crystals of m.p. 197° (from alcohol).

Found %: S 10.63, 10.70. $C_{14}H_{19}O_3N_3S$. Calculated %: S 10.36.

The ketone products (I-IX). To a solution of equimolecular quantities of the methyl ketone (0.01 g-mole) and of the aldehyde in a small quantity of alcohol (30 ml) there was gradually added with stirring a 5-10% solution of sodium hydroxide (2-5 ml). On the following day the precipitate was filtered off, washed with 70% aqueous alcohol, and recrystallized from aqueous alcohol (using activated charcoal) until a constant melting point was obtained.

The 2,4-dinitrophenylhydrazones of these ketones were obtained by mixing equimolecular quantities of an alcoholic solution of the unsaturated ketone with a hydrochloric acid solution of 2,4-dinitrophenylhydrazine and heating the mixture momentarily on a water bath. The precipitate was filtered off on the following day and washed with hydrochloric acid, alcohol, and ether; it was recrystallized from benzene or from glacial acetic acid until a constant melting point was obtained.

SUMMARY

1. Methods were developed for the formation of 2,4-dimethoxycinnamaldehyde, 2,4-dimethoxy- and 2,4,6-trimethoxybenzalacetones. Several of their derivatives are described.

2. A series of new thiophene analogs of di- and trimethoxychalcones and their vinyls have been obtained through the crotonic condensation, starting from 2-acetothienone, 2-thiophenaldehyde and 2-thiophenacetaldehyde. Their 2,4-dinitrophenylhydrazones and some physical and chemical properties are described.

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HETEROCYCLIC COMPOUNDS

SYNTHESIS OF BENZOATES OF γ - AND β -ISOMERS OF 1-(1-PHENYL-1-PROPENYL)-2,5-DIMETHYL-4-ETHYNYL-4-PIPERIDOL

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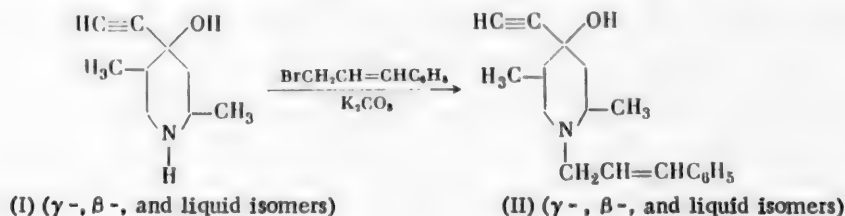
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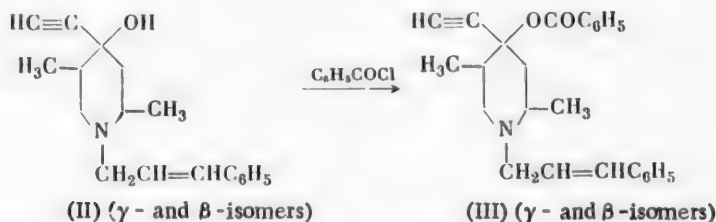
Original article submitted September 15, 1960

In previous communications [1, 2] there were described the benzoates of 1-alkenyl (alkyl) - 2,5-dimethyl-4-ethynyl-4-piperidols, which possess relatively high anesthetic power. In order to ascertain the effect of a phenyl group on the anesthetic activity of the esters, in the present work we synthesized the benzoates of the γ - and β -isomers of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II).

The initial individual isomers (γ -, β -, and liquid) of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II) were obtained with high yields (above 70%) by heating 1 mole of 2,5-dimethyl-4-ethynyl-4-piperidol (I) [3] with 1 mole of 1-phenyl-3-bromopropene-1 in acetone or ethanol solution with potassium carbonate [4, 5].



By esterification of the γ - and β -isomers of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II) with benzoyl chloride, the benzoates (III) were obtained.



EXPERIMENTAL

1-(1-Phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II). 1) γ -Isomer. A mixture of 3.1 g of the γ -isomer of 2,5-dimethyl-4-ethynyl-4-piperidol (m.p. 93-94°) [3], 40 ml of anhydrous acetone, and 5.5 g of anhydrous powdered potassium carbonate was placed in a three-necked flask fitted with a stirrer, reflux condenser, and dropping funnel; while stirring the mixture vigorously at 50°, a solution of 4.4 g of 1-phenyl-3-bromopropene-1 (b.p. 106-108° at 4 mm, n_D^{20} 1.6168, m.p. 31-32°) [6] was added dropwise over 30 minutes. The reaction mixture was stirred and heated 5 hours at 65-70° and then allowed to stand overnight. The precipitate was filtered off and washed several times with anhydrous ether. The acetone and the wash ether was distilled off, and the solidified residue was recrystallized three times from benzene (once by boiling with activated charcoal). Obtained 3.87 g (72%) of the γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II) with m.p. 113-114°.

A mixed sample with the initial piperidol melted at 75-87°.

Found %: N 5.16, 5.14. $C_{18}H_{23}ON$. Calculated %: N 5.19.

The hydrochloride was obtained from 2 g of the piperidol (m.p. 113-114°) dissolved in 5 ml of anhydrous acetone, adding an ether solution of dry hydrogen chloride up to acidic reaction to Congo. The precipitate was filtered off and recrystallized from anhydrous alcohol. Obtained 2.08 g (91.2%) of the hydrochloride of the γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol with m.p. 239-240°. A mixed sample with the hydrochloride of the initial piperidol melted at 169-177°.

Found %: N 4.30, 4.31. $C_{18}H_{24}ONCl$. Calculated %: N 4.55.

2) β -Isomer. To a mixture of 6.2 g of the β -isomer of 2,5-dimethyl-4-ethynyl-4-piperidol (m.p. 131-132°) [3], 50 ml of anhydrous alcohol, and 11 g of anhydrous powdered potassium carbonate, stirring at 60°, there was added dropwise over 30 minutes a solution of 8.6 g of 1-phenyl-3-bromopropene-1 in 10 ml of anhydrous alcohol. The mixture was heated with vigorous stirring for 5 hours at 75-80° and allowed to stand overnight. The precipitate was filtered off and washed thoroughly with anhydrous ether. The alcohol and the wash ether were distilled off, and the crystallized residue was recrystallized twice from acetone (once by boiling with charcoal). Obtained 8.1 g (75.3%) of the β -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (II) with m.p. 135-136°. A mixed sample with the initial piperidol melted at 97-103°.

Found %: N 5.56, 5.28. $C_{18}H_{23}ON$. Calculated %: N 5.19.

The hydrochloride of the piperidol was obtained by adding an ether solution of dry hydrogen chloride to an alcoholic solution of the base. From 0.25 g of the base, obtained 0.24 g of the hydrochloride with m.p. 223-224° (from alcohol). A mixed sample with the hydrochloride of the initial piperidol melted at 174-185°.

Found %: N 4.46, 4.27. $C_{18}H_{24}ONCl$. Calculated %: N 4.55.

3) Liquid isomer. A mixture of 2.3 g of the liquid isomer of 2,5-dimethyl-4-ethynyl-4-piperidol (n_D^{20} 1.4905) [3], 4 g of anhydrous potassium carbonate, 30 ml of anhydrous acetone, and 3.3 g of 1-phenyl-3-bromopropene-1 was heated 5 hours at 70-75°. The precipitate was separated and washed with ether, the wash ether and the acetone were distilled off, and the residue was vacuum distilled. Obtained 0.8 g of the liquid isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-3-piperidol (II) in the form of a thick liquid. B.p. 190-192° (2 mm), n_D^{20} 1.5460.

Found %: N 5.20, 5.24. $C_{18}H_{23}ON$. Calculated %: N 5.19.

Benzoate of γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (III). 1) A mixture of 1.35 g of the γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (m.p. 113-114°), 2.1 g of benzoyl chloride, and 7 ml of anhydrous pyridine was heated 15 hours at 100-110°, then after cooling was diluted with 10 ml of anhydrous ether and allowed to stand overnight. The precipitate was filtered off. Obtained 0.82 g of the hydrochloride of the benzoate of the γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (III) with m.p. 210-211.5° (from a 5 : 1 mixture of acetone and alcohol). A mixed sample with the hydrochloride of the initial piperidol melted at 198-204°.

Found %: N 3.40, 3.37. $C_{25}H_{28}O_2NCl$. Calculated %: N 3.41.

From the mother liquor, after distilling off the solvents and suitable treatment of the residue, obtained 0.2 g of the benzoate (III) in the form of the base, with m.p. 109-110° (from petroleum ether).

Found %: N 3.55, 3.75. $C_{25}H_{27}O_2N$. Calculated %: N 3.74.

The benzoate gave a mixed melting point of 88-93° with the initial piperidol, and gave a hydrochloride with m.p. 210-211.5°.

2) A mixture of 1.52 g of the hydrochloride of the γ -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol, 2.1 g of benzoyl chloride, and 7 ml of dry pyridine was heated 15 hours at 100-110°. Then the excess acid chloride and pyridine were distilled off under vacuum (aspirator); the residue after treatment with anhydrous ether and recrystallization weighed 1.24 g; m.p. 210-211.5° (from mixture of acetone and alcohol).

Benzoate of β -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (III). A mixture of 2.7 g of the β -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (m.p. 135-136°), 4.2 g benzoyl chloride, and 10 ml of anhydrous pyridine was heated 15 hours at 100-110°. By the method described above, the benzoate could not be separated successfully from the reaction mass in the form of a crystalline hydrochloride.

After distilling off the solvent and the excess acid chloride, the residue was treated with ether and with sodium carbonate solution; the separated base was extracted with ether. After drying with sodium sulfate and distilling off the ether, obtained 0.7 g of the benzoate of the β -isomer of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol (III) with m.p. 126-127° (from gasoline).

A mixed sample with the initial piperidol melted at 105-112°. The hydrochloride of the benzoate melted at 199-200°.

Found %: N 3.70, 3.71. $C_{25}H_{27}O_2N$. Calculated %: N 3.74.

A mixed sample with the hydrochloride of the initial piperidol melted at 175-184°, and with the hydrochloride of the benzoate of the γ -isomer of this piperidol (m.p. 210-211.5°) at 183-192°.

Found %: N 3.45, 3.40. $C_{25}H_{28}O_2NCl$. Calculated %: N 3.41.

SUMMARY

1. By the interaction of 1 mole of the γ -, β -, and liquid isomers of 2,5-dimethyl-4-ethynyl-4-piperidol with 1 mole of 1-phenyl-3-bromopropene-1 in acetone or ethanol with potassium carbonate, the corresponding isomers (γ , β , and liquid) of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol have been obtained.

2. The benzoates of the γ - and β -isomers of 1-(1-phenyl-1-propenyl)-2,5-dimethyl-4-ethynyl-4-piperidol have been synthesized.

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CYANINE DYES WITH UNSATURATED SUBSTITUENTS

IX. CARBOCYANINES AND MEROCYANINES CONTAINING PHENYL-ACETYLENYL RADICALS

I. K. Ushenko

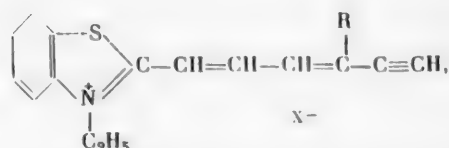
Institute of Organic Chemistry, Academy of Sciences, Ukr.SSR

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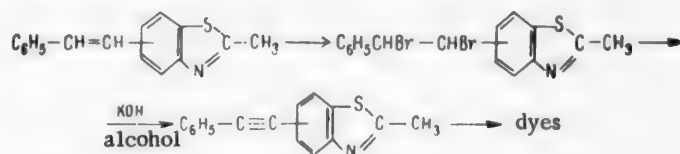
Original article submitted September 24, 1960

Recently we have prepared cyanine dyes containing various unsaturated substituents in their side chains [1-8] and have investigated their optical and photographic properties [8-12]. It was found that the introduction of unsaturated substituents into the heterocyclic rings of a cyanine dye molecule displaces the absorption band sharply toward the long-wave portion of the spectrum. Cyanine dyes with triple bonds in the molecule are in general unknown up to the present. Several years ago work was published in which triphenylmethane dyes containing a triple bond were reported [13-15]. Polymethine dyes containing an acetylene group are cited in a patent [16].



Recently a pyridodimethinemerocyanine has been synthesized containing a phenylacetylenyl radical on the pyridine ring [17]. These examples exhaust the literature on dyes containing a triple bond.

In the present communication cyanine dyes are described containing phenylacetylenyl radicals on benzothiazole and quinoline rings. The synthesis of such dyes was accomplished according to the scheme:

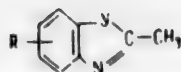


The bases which we obtained are listed in Table 1.

The ultraviolet absorption spectra of the bases synthesized are shown in Figs. 1-3. From the figures it is evident that on introducing styryl radicals into a quinaldine or 2-methylbenzothiazole molecule, an intense absorption band (K-band) appears in the near-ultraviolet, the nature of which is dependent on the conjugation of the heterocyclic ring with the unsaturated substituent (Figs. 1-3, curves 2, 5, 8). When the conjugation is destroyed by adding bromine to the double bond of the styryl group, the K-band disappears completely (curves 3, 6, 9).

On replacement of the styryl radicals by phenylacetylenyl radicals, all three absorption bands that are characteristic for styryl derivatives of 2-methylbenzothiazole and quinaldine are shifted toward the short-wave region of the spectrum (curves 4, 7, 10). At the same time, the intensity of absorption of the bases with the triple bond is somewhat less than the intensity of absorption of the corresponding styryl derivatives. In order to establish the presence of the triple bond, the infrared absorption spectra of these bases were taken. It is well known that there are primary bands in the $2260-2190\text{ cm}^{-1}$ region of the infrared spectra of disubstituted acetylenic hydrocarbons [18].

TABLE 1



Compound No.	R	Y	Position of substituent
(I)	$C_6H_5-CHBr-CHBr$	S	5
(II)	$C_6H_5-CHBr-CHBr$	S	6
(III)	$C_6H_5-CHBr-CHBr$	$-CH=CH-$	6
(IV)	$C_6H_5-C\equiv C$	S	5
(V)	$C_6H_5-C\equiv C$	S	6
(VI)	$C_6H_5-C\equiv C$	$-CH=CH-$	6

The infrared absorption spectra of compounds (IV) and (VI), taken on an IKS-12 spectrometer,* are shown in Fig. 4.

From Fig. 4 it is evident that for 2-methyl-5-phenylacetylenylbenzothiazole (IV) there are two bands in the infrared absorption spectrum, one at 2205 cm^{-1} ($4.52\text{ }\mu$) and the other at 2195 cm^{-1} ($4.58\text{ }\mu$); the latter is not very intense.

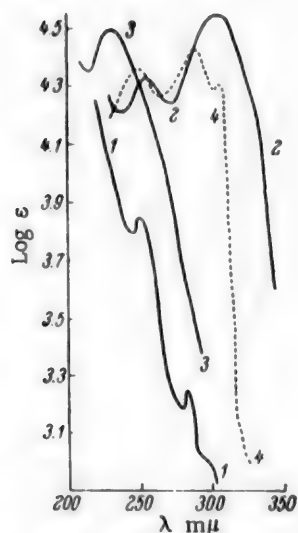


Fig. 1. UV absorption spectra. 1) 2-Methylbenzothiazole; 2) 2-methyl-5-styrylbenzothiazole; 3) 2-methyl-5-(α, β -dibromo- β -phenylethyl)-benzothiazole; 4) 2-methyl-5-phenylacetylenylbenzothiazole.

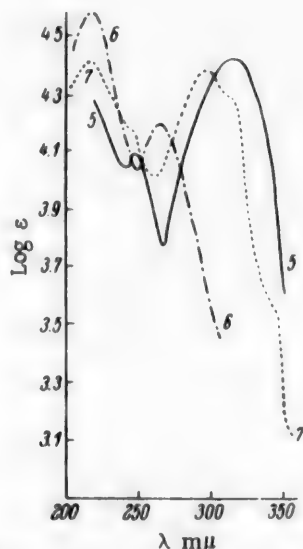


Fig. 2. UV absorption spectra. 5) 2-Methyl-6-styrylbenzothiazole; 6) 2-methyl-6-(α, β -dibromo- β -phenylethyl)-benzothiazole; 7) 2-methyl-6-phenylacetylenylbenzothiazole.

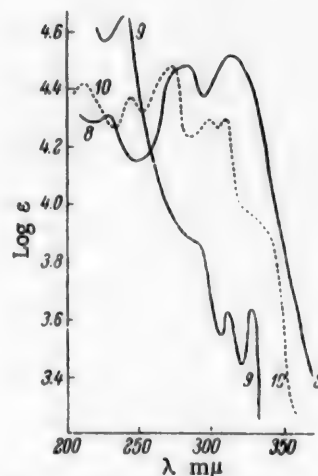
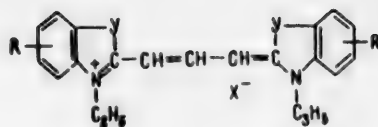


Fig. 3. UV absorption spectra. 8) 2-Methyl-6-styrylquinoline; 9) 2-methyl-6-(α, β -dibromo- β -phenylethyl)-quinoline; 10) 2-methyl-6-phenylacetylenylquinoline.

For 2-methyl-6-phenylacetylenylquinoline (VI), only one band was detected, at 2205 cm^{-1} ($4.52\text{ }\mu$). On heating the base with diethyl sulfate or ethyl p-toluenesulfonate, quaternary salts are formed which are readily condensed

* The measurements of the ultraviolet and infrared spectra were carried out by A. A. Kisilenko, for which we express our gratitude.

TABLE 2



Compound No.	R	Y	Position of substituent	Absorption max., μ	Hypsochromic shift, μ
— (VII) {	$C_6H_5-CH=CH-$	S	5.5'	582	} 8
	$C_6H_5-C\equiv C-$	S	5.5'	574	
— (VIII) {	$C_6H_5-CH=CH-$	S	6.6'	600	} 8
	$C_6H_5-C\equiv C-$	S	6.6'	592	
— (IX) {	$C_6H_5-CH=CH-$	$-CH=CH-$	6.6'	646 (596)	} 10
	$C_6H_5-C\equiv C-$	$-CH=CH-$	6.6'	636 (588)	

with orthoformic ester in pyridine, forming carbocyanines. The base (II) on heating with diethyl sulfate and subsequent condensation of the resulting quaternary salt with orthoformic ester in acetic anhydride medium,* gives 3,3'-diethyl-6,6'-bis(α,β-dibromo-β-phenylethyl)-thiacarbocyanine (absorption maximum 566 mμ).

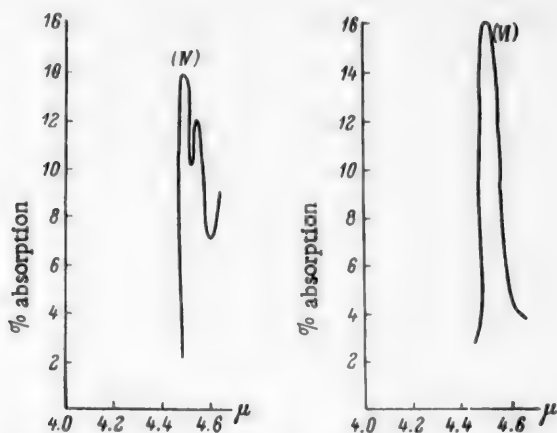


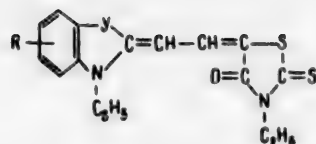
Fig. 4. IR absorption spectra. (IV) 2-Methyl-5-phenyl-acetylenylbenzothiazole; (VI) 2-methyl-6-phenylacetylenylquinoline.

The absorption maxima for certain carbocyanines containing phenylacetylenyl radicals are shown in Table 2. The absorption maxima of the corresponding distyrylcarbocyanines, which we obtained previously [1, 2, 4], are also shown for comparison. From these data it is evident that carbocyanines containing styryl groups on the heterocyclic rings absorb light at longer wave lengths than do the carbocyanines containing phenylacetylenyl radicals at the same positions.

At the same time, the magnitude of the hypsochromic shift for the 5,5' and 6,6' substituted thiacarbocyanines and for the 6,6'-diphenylacetylenylquinocarbocyanines is almost identical, and is equal to 8-10 mμ.

* If the condensation is carried out in pyridine, a blue-violet dye is formed. Probably hydrogen bromide is split out, forming a triple bond.

TABLE 3



Compound No.	R	Y	Position of substituent	Absorption max., mμ	Hypsochromic shift of absorption max., mμ
(X) {	C ₆ H ₅ -CH=CH-	S	5	531	} 5
	C ₆ H ₅ -C≡C-	S	5	526	
(XI) {	C ₆ H ₅ -CH=CH-	S	6	540	} 4
	C ₆ H ₅ -C≡C-	S	6	536	
(XII) {	C ₆ H ₅ -CH=CH-	-CH=CH-	6	584 (550)	} 4
	C ₆ H ₅ -C≡C-	-CH=CH-	6	580 (544)	

Analogous relationships are observed for the majority of the polyenes and polyynes; at the same time, the polyynes as a rule absorb light at a somewhat shorter wave length than do the polyenes [19].

The absorption curves of the carbocyanines with phenylacetylenyl groups are monotypic and in nature are entirely undistinguishable from the absorption curves of the dyes containing styryl groups. A difference exists only in the position of the absorption maxima.

The quaternary salts were also condensed with 3-ethyl-5-(acetanilidomethylene)-rhodanine in anhydrous alcohol in the presence of triethylamine; thereby merocyanines were obtained, as shown in Table 3.

From the data of Table 3 it is evident that replacing the styryl radicals by phenylacetylenyl radicals in the merocyanine molecule also causes a hypsochromic shift, equal to 4-5 mμ.

EXPERIMENTAL

2-Methyl-6-(α,β-dibromo-β-phenylethyl)-benzothiazole (II). A 2.5 g quantity of 2-methyl-6-styrylbenzothiazole [1] was dissolved in 25 ml of carbon tetrachloride. The solution was cooled to 5°, and 1.6 g bromine in 12 ml carbon tetrachloride was added in 2-3 portions. After adding all the bromine, the mixture was cooled 1.5 hr in ice water. The precipitate (2.14 g) was filtered off and dried. On the following day, another 0.16 g of the dibromide had precipitated from the mother liquor. Total yield 2.3 g (56%), m.p. 151-152°. After crystallization from 90 ml isobutanol, yield 1.7 g (41%), m.p. 171°. Lustrous, colorless needles.

Found %: Br 38.84, 39.00. C₁₆H₁₃NSBr₂. Calculated %: Br 35.58.

2-Methyl-5-(α,β-dibromo-β-phenylethyl)-benzothiazole (I). A 2.5 g quantity of 2-methyl-5-styrylbenzothiazole [2] was dissolved in 32 ml of carbon tetrachloride. The solution was cooled, and 1.6 g bromine in 12 ml carbon tetrachloride was added to it. The mixture was held in ice 2 hr; the precipitate was filtered off, washed with 4 ml methanol, and dried. Yield 2.44 g (59%), m.p. 167°. The dibromide was crystallized from isobutanol. Yield 1.6 g (40%). Lustrous colorless needles, m.p. 168-169°.

Found %: Br 38.72, 38.59. C₁₆H₁₃NSBr₂. Calculated %: Br 38.95.

Both in the first synthesis and in the second, after removing the carbon tetrachloride, there was obtained a viscous, noncrystalline mass of a dirty green color (probably perbromides), which was not investigated in detail.

2-Methyl-6-(α,β-dibromo-β-phenylethyl)-quinoline (III). A 2.45 g quantity of 2-methyl-6-styrylquinoline [7] was dissolved in 120 ml carbon tetrachloride* with heating. The solution was cooled, and at 35-40° there was

* If the reaction is conducted in chloroform, a dibromide with a lower melting point is obtained.

added 1.6 g bromine in 10 ml carbon tetrachloride. The mixture was allowed to stand until the following day. The carbon tetrachloride was driven off completely on a steam bath, and the residue was boiled with 15 ml alcohol; after cooling, the precipitate was filtered off and washed with alcohol. Weight 2.6 g, m.p. 135-138°. The dibromide was crystallized from 42 ml isobutanol. Yield 2.2 g (54%), m.p. 140-142°. A 0.5 g quantity of the dibromide was crystallized twice from alcohol, using bone black. Weight 0.3 g. Lustrous, colorless long needles, m.p. 141-143°.

Found %: Br 39.82, 39.91. $C_{18}H_{15}NBr_2$. Calculated %: Br 39.50.

2-Methyl-5-phenylacetylenylbenzothiazole (IV). A 6.15 g quantity of the dibromide (I) was added over 20-25 min to a boiling alcoholic KOH solution (4.2 g in 60 ml alcohol). Then the mixture was heated 3 hr on a steam bath. The alcohol was driven off, and the mixture was transferred to a beaker, using 70 ml of wash water; after cooling, the alkali was taken up with hydrochloric acid to a strictly neutral reaction. The base was extracted twice with benzene, after which the benzene was driven off on a steam bath. The resulting oil crystallized. This product was crystallized from alcohol, using bone black. Yield 2.4 g (64%), m.p. 122-123°. After a second crystallization from alcohol, obtained large tablets, m.p. 130-131°. Yield 1.8 g (48%). Colorless plates with a pearly luster, m.p. 130-131° (from alcohol-water mixture).

Found %: S 12.95, 12.94. $C_{16}H_{11}NS$. Calculated %: S 12.81.

2-Methyl-6-phenylacetylenylbenzothiazole (V). A 2.05 g quantity of the dibromide (II) was introduced into an alcoholic KOH solution (1.4 g in 20 ml alcohol). The mass was boiled 2 hr. After cooling, the precipitate was filtered off and washed on the filter with anhydrous alcohol. The alcohol was driven off completely, 70 ml of water was added to the residue, the base was extracted with ether, and the ether was driven off, leaving an oily residue that crystallized on standing. The base forms salts readily, and is very readily soluble in all organic solvents. Yield 0.55 g (44%). A 0.49 g quantity of the 2-methyl-6-phenylacetylenylbenzothiazole was dissolved in 8 ml methanol, and 0.45 g picric acid in 10 ml boiling methanol was added to the solution. After standing, yellow crystals precipitated. Lustrous, yellow plates, m.p. 161-162° (from alcohol).

Found %: N 11.60, 11.47. $C_{22}H_{14}O_7N_4S$. Calculated %: N 11.71.

2-Methyl-6-phenylacetylenylquinoline (VI). A 3 g quantity of 2-methyl-6-(α , β -dibromo- β -phenylethyl)-quinoline (III) was added over 20 min to a boiling alcoholic KOH solution (1.66 g in 25 ml alcohol), and the mixture was boiled 3 hr on a steam bath. The alcohol was driven off, and the residue was transferred to a beaker with 70 ml of wash water; the KOH was neutralized with dilute hydrochloric acid. The base was extracted with benzene, and the benzene was driven off on a steam bath. The residue was an oil, which crystallized. Yield 1.5 g (83%).

A 0.7 g quantity of the 2-methyl-6-phenylacetylenylquinoline was dissolved in 10 ml alcohol, and a solution of 0.65 g picric acid in 5 ml alcohol was added. The mixture was heated to boiling and allowed to stand until the following day. Then the picrate was filtered off. Yellow, lustrous tablets, m.p. 182-183° (from alcohol).

Found %: N 11.83, 11.64. $C_{22}H_{16}O_7N_4$. Calculated %: N 11.87.

To a suspension of 0.6 g of the picrate in 20 ml hot water, a solution of 0.36 g sodium acetate in 2 ml water was added. The mixture was heated with shaking for several minutes, until the base was melted. After cooling, the crystalline precipitate was broken up, filtered off, and dried. Weight 0.2 g, m.p. 97-98°. The base was dissolved in chloroform and chromatographed on aluminum oxide. The chloroform eluate was evaporated on a steam bath. Obtained 0.17 g of colorless tablets, m.p. 98-99°.

Dyes

3,3'-Diethyl-5,5'-di(phenylacetylenyl)-thiacarbocyanine ethylsulfate (VII). A mixture of 0.25 g 2-methyl-5-phenylacetylenylbenzothiazole (IV) and 0.17 g diethyl sulfate was heated in a paraffin bath at 140-150° (bath temperature) for 1.5 hr. To the quaternary salt there was added 0.5 g orthoformic ester and 2 ml dry pyridine, and the mixture was heated 35 min in the paraffin bath at 125-130°. On the following day, 10 ml ether was added to the residue, and the precipitate was filtered off, washed with a small quantity of alcohol and then with water, and then crystallized from alcohol. Yield 0.35 g (50%). Lustrous, dark-green tablets, m.p. 309-310°.

Found %: S 13.56, 13.45. $C_{39}H_{34}O_4N_2S_3$. Calculated %: S 13.91.

3,3'-Diethyl-6,6'-di(phenylacetylenyl)-thiacarbocyanine ethylsulfate (VIII). A mixture of 0.5 g 2-methyl-6-phenylacetylenylbenzothiazole (V) and 0.31 g diethyl sulfate was heated 1.5 hr at 140-145°. To the quaternary

salt there was added 0.8 g orthoformic ester and 3 ml anhydrous pyridine, and the mixture was boiled 20 min. The dye was precipitated with water and dried. Yield 0.3 g (21%). Dark-green crystals, m.p. 262-263° (from alcohol).

Found %: S 13.89, 13.98. $C_{39}H_{34}O_4N_2S_3$. Calculated %: S 13.91.

1,1'-Diethyl-6,6'-di(phenylacetylenyl)-quinocarbocyanine iodide (IX). A mixture of 0.48 g of 2-methyl-6-phenylacetylenylquinoline (VI) and 0.5 g ethyl p-toluenesulfonate was heated 2.5 hr at 145-150°. To the quaternary salt there was added 3 ml pyridine and 1 g orthoformic ester, and the mixture was boiled 25 min, after which it was precipitated with ether. The resulting viscous mass was dissolved in methanol. The dye was precipitated with potassium iodide, filtered off, and washed with warm water. Yield 0.25 g (36%). Fine, dark-colored crystals, m.p. 252-253° (from alcohol, decomp.).

Found %: N 4.11, 4.09. $C_{41}H_{33}N_2I$. Calculated %: N 4.11.

3-Ethyl-5-(3'-ethyl-5'-phenylacetylenylbenzothiazolinyldene-2'-ethylidene)-thiazolidinethione-2-one-4 (X). A mixture of 0.25 g of 2-methyl-5-phenylacetylenylbenzothiazole (IV) and 0.17 g diethyl sulfate was heated 1.5 hr at 140-145°. To the quaternary salt there was added 0.3 g of 3-ethyl-5-(acetanilidomethylene)-rhodanine, and the mixture was dissolved in 6 ml anhydrous alcohol. Triethylamine (0.5 ml) was added to the solution, and the mixture was boiled 15 min on a steam bath. After cooling, the precipitate was filtered off, washed with water and with methanol, and crystallized from benzene. Yield 0.27 g (65%). Lustrous, red tablets, m.p. 242-243° (decomp.).

Found %: S 21.40, 21.60. $C_{24}H_{20}ON_2S_3$. Calculated %: S 21.42.

3-Ethyl-5-(1'-ethyl-6'-phenylacetylenyldihydroquinolyldene-2'-ethylidene)-thiazolidinethione-2-one-4 (XII). A mixture of 0.48 g 2-methyl-6-phenylacetylenylquinoline (VI) and 0.5 g ethyl p-toluenesulfonate was heated 2.5 hr at 145-150°; then the salt was dissolved in 10 ml anhydrous alcohol. To the solution there was added 0.61 g 3-ethyl-5-(acetanilidomethylene)-rhodanine and 0.7 ml triethylamine, and the mixture was boiled 20 min on a steam bath. On the following day the precipitated dye was filtered off and washed with methanol. Yield 0.2 g (22%). Green tablets, m.p. 267° (from benzene, decomp.).

Found %: S 14.44, 14.34. $C_{26}H_{22}ON_2S_2$. Calculated %: S 14.47.

3,3'-Diethyl-5,5'-di(phenylacetylenyl)-9-methylthiacarbocyanine iodide (XIII). A mixture of 0.25 g 2-methyl-5-phenylacetylenylbenzothiazole (IV) and 0.17 g diethyl sulfate was heated 1.5 hr at 140-145°. To the quaternary salt there was added 0.5 g orthoacetic ester, 2 ml anhydrous pyridine, and 4 drops acetic anhydride, and the mixture was boiled 45 min. The reaction mass was poured into a hot aqueous solution of potassium iodide. The precipitate was filtered off, washed with water, dried, and crystallized from alcohol. Yield 0.22 g (31%). Fine, dark-green crystals, m.p. 277-278° (decomp.). Maximum absorption 560 mμ.

Found %: S 9.35, 9.53. $C_{38}H_{31}N_2S_2I$. Calculated %: S 9.06.

3,3',9-Triethyl-5,5'-di(phenylacetylenyl)-thiacarbocyanine iodide (XIV). A mixture of 0.25 g of the base and 0.17 g of diethyl sulfate was heated 1.5 hr at 140-145°. To the quaternary salt there was added 0.5 g orthopropionic ester and 2 ml anhydrous pyridine, and the mixture was boiled 40 min. Yield 0.2 g (27%). Fine, black crystals, m.p. 249-250° (decomp.). Absorption maximum 563 mμ.

Found %: S 9.15, 9.33. $C_{39}H_{33}N_2S_2I$. Calculated %: S 8.88.

SUMMARY

1. By addition of bromine to 2-methyl-5- or 2-methyl-6-styrylbenzothiazole and to 6-styrylquinoline, the corresponding dibromides have been prepared. By the action of alkali on the dibromides, there have been prepared 2-methyl-5-phenylacetylenylbenzothiazole, 2-methyl-6-phenylacetylenylbenzothiazole, and 6-phenylacetylenylquinoline.

2. Quaternary salts have been prepared from the bases, and carbocyanines and merocyanines from the quaternary salts.

3. It has been established that carbocyanines and merocyanines containing phenylacetylenyl radicals on the heterocyclic rings absorb light at shorter wave lengths than do the corresponding styryl-substituted carbocyanines and merocyanines.

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INVESTIGATIONS IN THE FIELD OF THE CHEMISTRY OF CYANINE DYES

XVII. SYNTHESIS OF ARYLBENZOTHAZOLES AND PREPARATION OF THEIR THIACARBOCYANINES

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Previously we had shown that diazo compounds of the benzothiazole series, when in nondissociating solvents, decompose with the formation of free benzothiazolyl radicals [1-3]. The latter, reacting with liquid aromatic hydrocarbons, form aryl-substituted benzothiazoles. It is indicated in the literature [4] that 1-aryl-3,3-dimethyl-1,3,4-thiadiazoles are good sources of free aryl radicals and can be utilized for the synthesis of unsymmetrical biaryls. We had reported certain dialkylbenzothiazolyltriazenes previously [3]. It was found that they are insoluble in water but readily soluble in benzene and other organic solvents. Their solutions are stable to alkalis, but are decomposed readily by mineral and organic acids, forming diazonium salts and dialkylamines. On passing a stream of dry hydrogen chloride through benzene solutions of benzothiazolyltrimethyltriazenes, phenylated derivatives of benzothiazole are formed readily. The dry hydrogen chloride may be replaced by glacial acetic acid, which gives a somewhat higher yield of phenylbenzothiazoles and a considerable simplification in the method of preparing arylbenzothiazoles.

An additional advantage of this method of arylating benzothiazoles, in comparison with the diazoacetate method [1], is that the decomposition of the benzothiazolyltrimethyltriazenes can be carried out not only in a medium of liquid aromatic compounds, but also in melts of substances that are solid at room temperature but melt at 90-100°.

The syntheses of certain arylbenzothiazoles and of cyanine dyes derived from them are set forth below. By the interaction of diazotized 2-methyl-6-aminobenzothiazole with nitrobenzene in the presence of sodium acetate, a mixture was obtained consisting of 2-methyl-6-(p-nitrophenyl)- and apparently 2-methyl-6-(o-nitrophenyl)-benzothiazole (compare [5]), which was purified by chromatography on aluminum oxide. The yield of 2-methyl-6-nitrophenylbenzothiazole with m.p. 152-153° was 23%. From the mother liquor another isomer was recovered with m.p. 55-62°, yield 16%.

For establishing the structure of the products obtained, we made use of a method described in the literature [6]. The 2-methylnitrophenylbenzothiazole (m.p. 152-153°) was split with hydrazine hydrate, and the resulting aminothiophenol was oxidized to the disulfide. The resulting 5,5'-bis(nitrophenyl)-2,2'-diaminodiphenyl disulfide was subjected to oxidation, as a result of which p-nitrobenzoic acid was obtained. Hence it follows that the isomer with m.p. 152-153° is 2-methyl-6-(p-nitrophenyl)-benzothiazole.

Analogously, from 2-methyl-5-aminobenzothiazole and nitrobenzene, a 2-methyl-5-nitrophenylbenzothiazole was obtained with m.p. 161-162° (21%), and a 2-methyl-5-nitrophenylbenzothiazole with m.p. 58-60° (19%). As a result of splitting and oxidation of the 161-162° m.p. isomer, p-nitrobenzoic acid was obtained. Thus, the isomer with m.p. 161-162° is 2-methyl-5-(p-nitrophenyl)-benzothiazole. The synthesis of the nitrophenylbenzothiazoles can be represented by the following scheme:

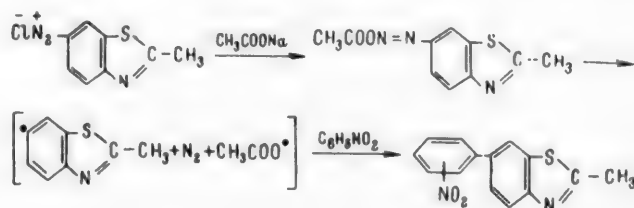
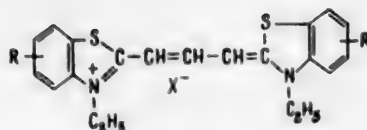


TABLE 1

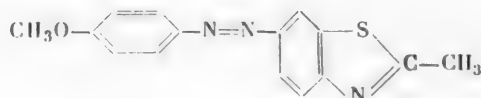


Position of substituent	R	Absorption max., mμ	Shift of absorption max., mμ
	H	558	—
6.6'	OCH ₃	573	+15
6.6'	OH	575	+17
6.6'	O ⁻	618	+60
6.6'	SCH ₃	581	+23
6.6'	NO ₂	584	+26
6.6'	NHCOCH ₃	581	+23
6.6'	C ₆ H ₅	574 *	+16
6.6'	C ₆ H ₄ OCH ₃ -p	580	+22
6.6'	C ₆ H ₄ OH-p	581	+23
6.6'	C ₆ H ₄ O ⁻	585	+27
6.6'	C ₆ H ₄ SCH ₃ -p	580	+22
6.6'	C ₆ H ₄ NO ₂ -p	581	+23
6.6'	C ₆ H ₄ NHCOCH ₃ -p	576	+18
5.5'	NO ₂	560	+2
5.5'	C ₆ H ₅	570 *	+12
5.5'	C ₆ H ₄ NO ₂ -p	570	+12
5.5'	C ₆ H ₄ NHCOCH ₃ -p	570	+12

* Dyes were prepared by N. N. Sveshnikov.

The resulting nitrophenylbenzothiazoles were reduced to the amines. From 2-methyl-6-(p-aminophenyl)-benzothiazole, by the Sandmeyer reaction, there was obtained 2-methyl-6-(p-hydroxyphenyl)-benzothiazole, and then 2-methyl-6-(p-methoxyphenyl)-benzothiazole. This route of synthesis proved to be a complex method for the preparation of 2-methyl-6-(p-methoxyphenyl)-benzothiazole; therefore, an attempt was made to synthesize this product by the decomposition of 2-methylbenzothiazolyl-6-diazonium acetate in anisole.

It was found that the anisole adds readily to the diazonium acetate, forming 2-methyl-6-(p-anisylazo)-benzothiazole:



There are several examples shown in the literature in which the interaction of aryldiazonium acetates with anisole results in the formation of methoxybiphenyls [7].

When utilizing triazenes of the benzothiazole series [3], it was found that the triazenes have less tendency toward the addition reaction than do the diazonium acetates. On heating 2-methylbenzothiazolyl-6-dimethyltriazene with anisole in the presence of glacial acetic acid, a mixture of 2-methyl-6-anisylbenzothiazoles was obtained in the form of a colorless thick oil, which partially crystallized on standing. Probably these crystals are the p-isomer, 2-methyl-6-p-anisylbenzothiazole. Analogously, from 2-methylbenzothiazolyl-6-dimethyltriazene and methyl phenyl sulfide (thianisole) in the presence of glacial acetic acid, a mixture of 2-methyl-6-methylmercaptophenylbenzothiazoles was obtained.

The 2-methylarylbenzothiazoles on heating with ethyl p-toluenesulfonate were converted to quaternary salts, and the latter to thiocarbocyanines. The dyes that we obtained were poorly crystallized, owing to their high molecular

weights; therefore, they were purified by chromatography on aluminum oxide with subsequent crystallization from alcohol.

Table 1 shows the absorption maxima of the diarylthiacarbocyanines. Absorption maxima are also given for comparison on thiocarbocyanines containing polar substituents and phenyl radicals at the 5,5' and 6,6' positions.

From the data of Table 1 it is evident that electron-donor and electron acceptor groups occurring directly on the benzothiazole rings give rise to a rather strong bathochromic shift. The introduction of hydroxy, methoxy, methylmercapto, acetylmino, and nitro groups into the para-position of the phenyl radical of 6,6'-diphenylthiacarbocyanine gives rise to hardly any additional deepening of color. Thus, when a benzene ring is interposed between the polar substituents and the benzothiazole ring, a weakening of the polar substituents' effect is observed. Such an observation can be explained on the basis of the work of Kiprianov [8] and Brooker [9], which showed that a benzene ring included in a polymethine chromophore of a cyanine dye tends to retain the benzene structure. This hinders the development of the conjugation effect responsible for an observed color increase.

EXPERIMENTAL

2-Methyl-5-aminobenzothiazole [10] and 2-methyl-6-aminobenzothiazole [11] were prepared by the methods described previously. Thiophenol was prepared by the reduction of benzenesulfonyl chloride with zinc dust [12]. Methyl phenyl sulfide (thianisole) was prepared by methylation of thiophenol with dimethyl sulfate in alkaline medium [13]. Yield 88%; m.p. 186-188°.

2-Methylbenzothiazolyl-6-dimethyltriazene. A 9.8 g quantity of 2-methyl-6-aminobenzothiazole was dissolved in 20 ml hydrochloric acid (d. 1.19) and 15 ml water. The solution was cooled to -5°, and the paste of crystals was diazotized with 4.4 g sodium nitrite in 7 ml water. After 5-10 min the diazo solution was poured into a chilled dropping funnel. A 9.6 g quantity of a 33% solution of dimethylamine in absolute alcohol was poured into a chilled solution of 27 g calcined sodium carbonate and 150 ml water, and the benzothiazolylidiazonium chloride was added to the resulting solution at -2°, over a 20 min period, with vigorous stirring. Then the mixture was stirred 1 hr; the precipitate was filtered off, air-dried, and extracted with 80 ml chloroform; the chloroform was driven off, and the solid residue was once again extracted with hot petroleum ether, which was then completely driven off. Yield 11.7 g (89%). Finally, the dimethyltriazene was crystallized from petroleum ether. Yield 70%; yellow-orange crystals, m.p. 74°.

Found %: N 25.78, 25.80. $C_{10}H_{12}N_4S$. Calculated %: N 25.45.

2-Methylbenzothiazolyl-5-dimethyltriazene was obtained by an analogous method from 9.8 g of 2-methyl-5-aminobenzothiazole. Yield after crystallization 10.4 g (78%). Lustrous, light orange tablets, m.p. 111° (from petroleum ether).

Found %: N 25.36, 25.40. $C_{10}H_{12}N_4S$. Calculated %: N 25.45.

2-Methylmercaptobenzothiazolyl-6-dimethyltriazene. An 11.7 g quantity of 2-methylmercapto-6-aminobenzothiazole was dissolved in 42 ml hydrochloric acid (d. 1.19) and 35 ml water. The solution was cooled to -2° and diazotized with 4.9 g sodium nitrite in 8 ml water. A second solution was prepared from 56 g anhydrous sodium carbonate, 520 ml water, and 9.6 g of a 33% solution of dimethylamine in absolute alcohol. Then the solutions were mixed together. The precipitated triazene, after drying, was dissolved in chloroform and filtered, and the chloroform was completely driven off.

Yield 13 g (86%). Light orange tablets, m.p. 69-70° (from petroleum ether).

Found %: N 22.17, 22.00. $C_{10}H_{12}N_4S_2$. Calculated %: N 22.22.

2-Ethylbenzothiazolyl-6-dimethyltriazene. A 10.6 g quantity of 2-ethyl-6-aminobenzothiazole [11] was dissolved in 15 ml water and 20 ml concentrated hydrochloric acid. The solution was cooled to -5° and diazotized with 4.5 g sodium nitrite in 7 ml water. Then the diazonium chloride was added over 15 min to a chilled mixture of 9.5 g of 33% dimethylamine solution and 27 g sodium carbonate in 250 ml water. After 1 hr stirring, a thick oil was separated from the aqueous layer and extracted with chloroform, the chloroform was driven off, the triazene was dissolved in hot petroleum ether, the solution was separated from the tar and filtered, and the petroleum ether was driven off. Thick, yellow oil; yield 9.5 g (65%). The triazene could not be vacuum distilled, since it decomposed.

Found %: N 22.85. $C_{11}H_{14}N_4S$. Calculated %: N 23.93.

Benzothiazolyl-2-dimethyltriazene. A 6 g quantity of 2-aminobenzothiazole was dissolved in 30 ml glacial acetic acid and cooled to -2° . A 3.2 g quantity of sodium nitrite was added with stirring to 25 ml concentrated sulfuric acid, cooled to -2° . Then the thick mass of the 2-aminobenzothiazole was added with vigorous stirring to the nitrosyl sulfuric acid. The diazo solution was held 5 min and diluted with 15 ml cold water. Then the diazonium chloride was added over 20 min to a chilled mixture consisting of 54 g sodium carbonate, 520 ml water, and 6.7 g of a 33% dimethylamine solution. It was necessary to carry out the reaction in a 2 liter wide beaker. After standing 1 hr, the precipitate was filtered off, washed with water, dried, dissolved in boiling chloroform, and filtered, and the chloroform was driven off completely. Yield 4.5 g (65%). Fine orange crystals, m.p. $176-177^{\circ}$ (from ligroin; decomp.).

Found %: N 26.33, 26.28. $C_9H_{10}N_4S$. Calculated %: N 27.18.

2-Methyl-6-(p-nitrophenyl)-benzothiazole. A 19.7 g quantity of 2-methyl-6-aminobenzothiazole was dissolved in 40 ml concentrated hydrochloric acid and 30 ml water. The solution was cooled to -4° and diazotized with 8.8 g sodium nitrite in 15 ml water. The diazonium chloride, after 5 min standing, was poured into 400 ml nitrobenzene, cooled to $+7^{\circ}$. The mixture was stirred vigorously, and a solution of 54 g crystalline sodium acetate in 150 ml water was added to it over 40 min. Then the mixture was stirred 3 hr at $6-7^{\circ}$ and 28 hr at 24° . The nitrobenzene was removed by steam distillation; the residue after hardening was crushed, washed with water, dried, and dissolved in chloroform, and the solution was filtered through aluminum oxide (length of tube 20 cm, diameter 4.5 cm). The eluate was concentrated and chromatographed four times on aluminum oxide for the removal of colored products. The elution was performed with benzene. Yield 12.8 g (40%). Light yellow crystals, m.p. $70-96^{\circ}$. Then the mixture of isomers was subjected to crystallization from methanol until a constant melting point was reached. Yield of 2-methyl-6-nitrobenzothiazole with m.p. $152-153^{\circ}$, 7.5 g (23%). Light yellow needles.

Found %: N 10.33, 10.12. $C_{14}H_{10}O_2N_2S$. Calculated %: N 10.37.

Establishing the structure of the 2-methyl-6-nitrophenylbenzothiazole with m.p. $152-153^{\circ}$. A 2.7 g quantity of the 2-methyl-6-nitrophenylbenzothiazole was dissolved in 100 ml alcohol, and 40 ml of hydrazine hydrate was added to the solution. The mixture was boiled 4 hr, the alcohol was driven off, the residue was diluted with 100 ml water, and 150 ml of a 2% hydrogen peroxide solution was added with cooling. The mixture stood until the following day; then 35-40 ml of aqueous saturated potassium chloride solution was added, and the yellow-orange precipitate was filtered off, washed with water, and dried. Yield of 5,5'-bis(nitrophenyl)-2,2'-diaminodiphenyl disulfide 2.1 g (42%). Reddish-orange tablets, m.p. $180-181^{\circ}$ (from butyl alcohol).

Found %: N 11.38, 11.49. $C_{24}H_{18}O_4N_4S_2$. Calculated %: N 11.43.

A 0.68 g quantity of this disulfide was dissolved in 30 ml glacial acetic acid, into which 3.2 g of chromium anhydride was introduced. The mixture was boiled 11 hr and then diluted with 100 ml water; the solution was evaporated to dryness on a steam bath, the residue was treated with 40 ml hot 10% sodium hydroxide solution, and the green-colored precipitate (chromic oxide) was filtered off and washed with 10 ml boiling water. The alkaline solution was neutralized (with cooling) with hydrochloric acid. Precipitate, light green color (0.2 g), m.p. $237-238^{\circ}$ (from water). A mixed sample with p-nitrobenzoic acid did not show any melting point depression. Thus, the base with m.p. $152-153^{\circ}$ is 2-methyl-6-(p-nitrophenyl)-benzothiazole.

2-Methyl-6-(p-acetylamino-phenyl)-benzothiazole. A 6.7 g quantity of 2-methyl-6-(p-nitrophenyl)-benzothiazole was dissolved in 110 ml methanol, and to the solution there was added 37 g stannous chloride dissolved in 50 ml concentrated hydrochloric acid. The mixture was heated 2.5 hr on a steam bath, the alcohol was driven off, and 50 ml water was added to the residue, plus sufficient 40% sodium hydroxide solution to dissolve the tin salts completely. The precipitated amine was filtered off, dissolved in methanol, and filtered; the alcohol was driven off on a steam bath, the amine was dissolved in 40 ml benzene, 7 g acetic anhydride was added to the solution, and the mixture was boiled 2 hr on the steam bath. The benzene was partially driven off, and the product that precipitated on cooling was filtered off. Yield 5.6 g (80%). After crystallization from benzene, obtained colorless tablets with m.p. $185-186^{\circ}$.

2-Methyl-5-(p-nitrophenyl)-benzothiazole. A 19.7 g quantity of 2-methyl-5-aminobenzothiazole was dissolved in 40 ml concentrated hydrochloric acid and 40 ml water. The solution was cooled to -5° and diazotized as indicated above. The recovery and purification of the 2-methyl-5-nitrophenylbenzenethiazoles was carried out analogously to that described above. Yield 14.1 g (44%). Light yellow crystals, m.p. $75-94^{\circ}$. The mixture of isomers was subjected to crystallization from methanol until the melting point remained constant. Yield of 2-methyl-5-nitrophenylbenzothiazole with m.p. $161-162^{\circ}$, 7 g (21%).

Found %: N 10.29, 10.15. $C_{14}H_{10}O_2N_2S$. Calculated %: N 10.37.

From the mother liquor, after removing the alcohol, there was obtained 6.3 g (19%) of a mixture of 2-methyl-5-nitrophenylbenzothiazoles with m.p. 58-69°.

Establishing the structure of the 2-methyl-5-nitrophenylbenzothiazole with m.p. 161-162°. A 0.81 g quantity of the 2-methyl-5-nitrophenylbenzothiazole was dissolved in 50 ml alcohol, and 15 ml hydrazine hydrate was added to the solution. Further treatment of the reaction mixture was carried out the same as that indicated for the 2-methyl-6-nitrobenzothiazole. Yield of 4,4'-bis(nitrophenyl)-2,2'-diaminodiphenyl disulfide 0.7 g. Yellow-orange tablets, m.p. 188-189° (from butyl alcohol).

Found %: N 11.24, 11.14. $C_{24}H_{18}O_4N_4S_2$. Calculated %: N 11.43.

A 0.49 g quantity of this disulfide was dissolved in 18 ml glacial acetic acid, and 2.5 g chromic anhydride was introduced into the solution. The mixture was boiled 7 hr. As a result of the oxidation, p-nitrobenzoic acid was obtained. Thus, the product with m.p. 161-162° is 2-methyl-5-(p-nitrophenyl)-benzothiazole.

2-Methyl-5-(p-acetylamino-phenyl)-benzothiazole. A 2.7 g quantity of 2-methyl-5-(p-nitrophenyl)-benzothiazole was dissolved in 60 ml methanol, and 14 g stannous chloride in 20 ml concentrated hydrochloric acid was added to the solution. The amine that was obtained was dissolved in 30 ml benzene, 3 g acetic anhydride was added to the solution, and the mixture was boiled 3 hr. After driving off the benzene, the product was poured into hot water, and the precipitate was filtered off. Yield 2.3 g (80%). Large colorless tablets, m.p. 171-172° (from 50% methanol).

Preparation of 2-methyl-6-(p-anisyl)-benzothiazole by decomposition of 2-methylbenzothiazolyl-6-dimethyl-triazene in anisole. An 11 g quantity of 2-methylbenzothiazolyl-6-dimethyltriazene was dissolved in 300 ml anisole, 50 ml glacial acetic acid (b.p. 118°) was added to the solution, and the mixture was heated 15 hr at 95-100°. The anisole was removed completely by steam distillation, the water was separated off (after cooling), and the dark brown residue was dissolved in chloroform and chromatographed on aluminum oxide. The zone formed by the 2-methyl-6-anisylbenzothiazoles showed a strong blue fluorescence under an ultraviolet lamp. The almost colorless zone was eluted with chloroform. Obtained a colorless oil. Yield 7.1 g (56%). A second experiment was set up with the same quantities of reactants. Yield of base 6.8 g. The products obtained in the first and second experiments were combined. After standing 3 days, the oil partially crystallized. Methanol (0.5 ml) was added to the mass, and the crystals were filtered off and thoroughly pressed. Colorless crystals; yield 5.6 g (22%), m.p. 73-74°. After crystallization from petroleum ether, the base melted at 77-78°. Weight of oil 7.4 g.

The picrate of the 2-methyl-6-(p-anisyl)-benzothiazole was obtained by dissolving 0.76 g of the benzothiazole (m.p. 73-74°) in 5 ml methanol and adding 0.68 g picric acid in 5 ml hot alcohol. Yield 0.8 g. Lemon-yellow tablets, m.p. 168-169° (from alcohol).

Found %: N 11.71, 11.82. $C_{21}H_{16}O_8N_4S$. Calculated %: N 11.57.

Preparation of 2-methyl-6-(p-methylmercaptophenyl)-benzothiazole by decomposition of 2-methylbenzothiazolyl-6-dimethyltriazene in thioanisole. An 11 g quantity of 2-methylbenzothiazolyl-6-dimethyltriazene was dissolved in 150 ml methyl phenyl sulfide, and 50 ml glacial acetic acid was added to the solution. The mixture was heated 23 hr at 95-100°. The recovery and purification of the bases was carried out as indicated above. Benzene was used for elution. Obtained a thick, colorless oil. Yield 5.6 g (41%). The oil partially crystallized after standing 4 days. Methanol (0.3 ml) was added to the mass, after which the colorless crystals were filtered off. Yield 2.8 g (20%), m.p. 86-87° (from methanol).

Found %: N 5.14, 5.21. $C_{15}H_{13}NS_2$. Calculated %: N 5.16.

Ethyl p-toluenesulfonate of 2-methyl-6-(p-nitrophenyl)-benzothiazole. A 1.3 g quantity of 2-methyl-6-(p-nitrophenyl)-benzothiazole and 2 g ethyl p-toluenesulfonate were heated in a paraffin bath 7 hr at 155-160° (bath temperature). The contents of the flask were dissolved in hot water, the aqueous solution was extracted with benzene, and the aqueous layer was separated, boiled with bone black, and evaporated on a steam bath. Then the salt was heated to 125-130°, with stirring. Yield 2.1 g (77%).

All of the other ethyl p-toluenesulfonates were obtained under analogous conditions. The yields of the quaternary salts reached 90%.

TABLE 2. Thiocarboyanines with Aromatic Substituents on the Benzothiazole Ring

Dye No.	Name of dye	Starting materials (g)		Condensing substance(mn)	Time of boiling(mn)	Yield (%)	M. p.	Analysis				
		quaternary salt	ortho-ester					found		calculated		
						ele-ment %	con-tent %	empirical formula	ele-ment %	con-tent %		
(I)	3,3'-Diethyl-6,6'-di(p-nitrophenyl)-thiocarbocyanine chloride	A-0.47	I-0.5	5	—	31	206°	N	9.05	C ₃₃ H ₂₇ O ₄ N ₄ S ₂ Cl	N	8.72
(II)	3,3'-Diethyl-5,5'-di(p-nitrophenyl)-thiocarbocyanine chloride	B-0.47	I-0.5	5	—	35	195	N	8.78	C ₃₃ H ₂₇ O ₄ N ₄ S ₂ Cl	N	8.72
(III)	3,3'-Diethyl-6,6'-di(p-acetylamino-phenyl)-thiocarbocyanine iodide	C-0.48	I-0.5	—	2	37	183	N	7.31, 7.29	C ₃₇ H ₃₅ O ₂ N ₄ S ₂ I	N	7.38
(IV)	3,3'-Diethyl-5,5'-di(acetylamino-phenyl)-thiocarbocyanine iodide	D-0.48	I-0.5	—	2	24	182	N	7.44, 7.57	C ₃₇ H ₃₅ O ₂ N ₄ S ₂ I	N	7.38
(V)	3,3'-Diethyl-6,6'-Di(p-anisyl)-thiocarbocyanine iodide	E-0.9	I-0.9	6	—	37	219	I	17.95, 18.08	C ₃₅ H ₃₃ O ₂ N ₂ S ₂ I	I	17.96
(VI)	3,3'-Diethyl-6,6'-Di(p-methylmercaptophenyl)-thiocarbocyanine iodide	F-0.47	I-0.5	3	—	17	226*	I	17.17, 16.97	C ₃₅ H ₃₃ N ₂ S ₄ I	I	17.24
(VII)	3,3'-Diethyl-6,6'-Di(p-hydroxyphenyl)-thiocarbocyanine perchlorate	G-0.44	I-0.5	3	—	30	225*	N	4.35, 4.11	C ₃₃ H ₂₉ O ₆ N ₂ S ₂ Cl	N	4.31

* Melting point with decomposition.

General method of synthesis of thiacyanines. For preparing the thiacyanines, a mixture of the ethyl p-toluenesulfonate of the appropriate 2-methyl-5- or 6-arylbenzothiazole, dry pyridine, and ortho-ester was boiled for a determined time. In some cases the addition of acetic anhydride increased the yield of dye considerably. After the heating period, the reaction mixture was poured at once into a hot aqueous solution of potassium chloride, bromide, or iodide, or of sodium perchlorate. The precipitated dye was filtered off, washed with water, dried, and subject to chromatography on aluminum oxide or crystallized from alcohol.

The conditions of synthesis of the thiacyanines and the results are shown in Table 2. The following conventional symbols are adopted in the table. Ethyl p-toluenesulfonates: of 2-methyl-6-(p-nitrophenyl)-benzothiazole (A), 2-methyl-5-(p-nitrophenyl)-benzothiazole (B), 2-methyl-6-(p-acetylaminophenyl)-benzothiazole (C), 2-methyl-5-(p-acetylaminophenyl)-benzothiazole (D), 2-methyl-6-(p-anisyl)-benzothiazole (E), 2-methyl-6-(p-methylmercaptophenyl)-benzothiazole (F), and 2-methyl-6-(p-hydroxyphenyl)-benzothiazole (G). Orthoformic ester (I), orthoacetic ester (II), and orthopropionic ester (III).

SUMMARY

1. It has been established that 2-methylnitrophenylbenzothiazoles are formed on the interaction of benzothiazolyldiazonium chlorides with nitrobenzene in the presence of sodium acetate. By means of fractional crystallization from the mixture of isomers [o- and p-], 2-methyl-6-(p-nitrophenyl)- and 2-methyl-5-(p-nitrophenyl)-benzothiazoles have been isolated and their structures established.
2. By the interaction of 2-methylbenzothiazolyl-6-dimethyltriazene with anisole and thioanisole, there have been obtained 2-methyl-6-(p-anisyl)-benzothiazole and, apparently, 2-methyl-6-(p-methylmercaptophenyl)-benzothiazole.
3. The synthesized 2-methylarylbenzothiazoles form quaternary salts readily on heating with ethyl p-toluenesulfonate. From the quaternary salts, by condensation with ortho-esters of carboxylic acids, thiacyanines have been obtained, containing various functional groups on the aryl radicals.
4. It has been established that the introduction of functional groups at the para position of the phenyl radical of 6,6'-diphenylthiacyanine causes almost no additional deepening of color.

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INVESTIGATIONS IN THE FIELD OF THE CHEMISTRY OF CYANINE DYES

XVIII. CONDENSATION OF AROMATIC AND ALICYCLIC KETONES WITH QUATERNARY SALTS OF 2-METHYLBENZOTHAIOLE, AND CONVERSION OF THE RESULTING COMPOUNDS INTO CYANINE DYES

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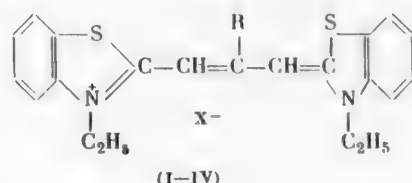
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

pp. 2869-2876, September, 1961

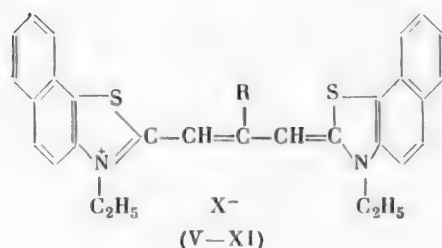
Original article submitted September 24, 1960

We had shown previously that various aromatic and heterocyclic ketones enter into condensation with quaternary salts of 2-methylbenzothiazole, forming quaternary salts of β -substituted 2-propenylbenzothiazoles [1-4]. The latter, being vinylenes homologs of 2-methylbenzothiazole, contain an active methyl group, and enter into a different type of condensation, forming 9-substituted thiacarboyanines, thiadicarboyanines, tetramethinemercocyanines, styryl dyes, and tricarboyanines [3, 4].

Continuing the investigations in this direction, we attempted to condense the following ketones with quaternary salts of substituted 2-methylbenzothiazole: p-methoxyacetophenone, o-methoxyacetophenone, o-nitroacetophenone, m-nitroacetophenone, and γ -acetylpyridine. It was found that o-nitroacetophenone and m-nitroacetophenone condense poorly with the ethyl p-toluenesulfonate of 2-methylbenzothiazole, and γ -acetylpyridine does not condense at all. The quaternary salts of β -substituted 2-propenylbenzothiazole that we synthesized were reacted with quaternary salts of 2-methylmercaptobenzothiazole, thereby obtaining thiacarboyanines (I-XI).



- (I) R = H, λ mp 559;
- (II) R = C₆H₅, λ mp 561;
- (III) R = C₆H₄NO₂-o, λ mp 569;
- (IV) R = C₆H₄NO₂-m, λ mp 566.



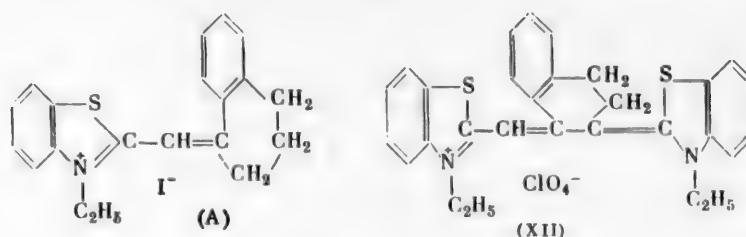
- (V) R = H, λ mp 594;
- (VI) R = C₆H₄OCH₃-p, λ mp 595;
- (VII) R = C₆H₄OH-p, λ mp 595;
- (VIII) R = C₆H₄O-p, λ mp 594;
- (IX) R = C₆H₄OCH₃-o, λ mp 597;
- (X) R = C₆H₄OH-o, λ mp 598;
- (XI) R = C₆H₄O-o, λ mp 597.

From these data it is evident that the absorption maxima of 9-arylthiacarboyanines differ little from that of the unsubstituted thiacarboyanine. It is peculiar that adding alkali solution to alcoholic solutions of 9-hydroxyphenyldibenzothiacarboyanines gives no change whatever in the absorption maxima. It had been shown previously [4, 5] that a phenyl group or various aromatic radicals occurring at the meso-position of a thiacarboyanine do not exert any material influence on the absorption maximum of the dye. Probably a phenyl group occurring at the 9-position of a thiacarboyanine experiences steric hindrance, as a result of which it leaves the plane of the benzo-

thiazole rings and cease to influence the light absorption. To eliminate this type of phenomenon, we decided to obtain thiacyanines for which the phenyl group would be fixed in the plane of the benzothiazole rings by means of methylene groups. For this purpose, indanone-1 and α -tetralone were brought into condensation with quaternary salts of 2-methylbenzothiazole. On heating indanone-1 with the ethyl p-toluenesulfonate of 2-methylbenzothiazole in the presence of acetic anhydride, and also with the addition of anhydrous potassium or sodium acetate, the corresponding propenyl derivatives were not obtained.

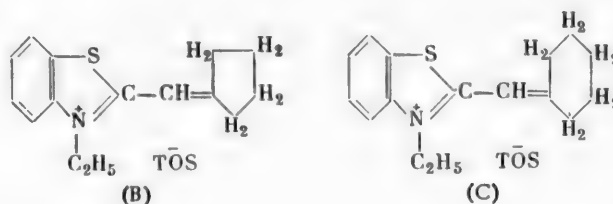
We encountered great difficulties during the separation of the reaction mixture obtained on condensation of the ethyl p-toluenesulfonate of 2-methylbenzothiazole with α -tetralone. Based on the results of several experiments, conditions were chosen for recovering and purifying the reaction product, after which the ethiodide (A) was obtained with 15% yield.

The quaternary salt (A) was brought into condensation with the ethiodide of 2-methylmercaptobenzothiazole, as a result of which the dye (XII) was obtained, with λ_{\max} 616 m μ .

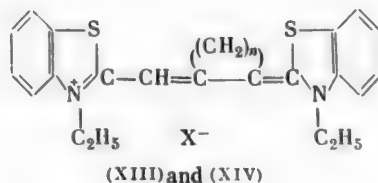


Thus, fixing the phenyl in the plane of the benzothiazole rings by means of methylene groups gives rise to a bathochromic effect equal to 57 m μ . On condensing the quaternary salt (A) with the ethiodide of 2-acetanilidovinylbenzothiazole and with 3-ethyl-2-formylmethylenbenzothiazoline, the corresponding thiacyanines were not obtained.

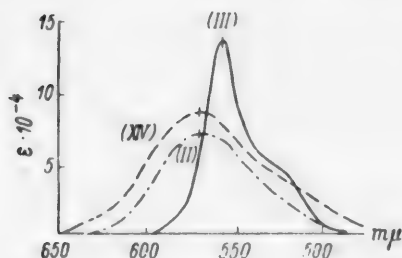
We also condensed the quaternary salts of 2-methylbenzothiazole with other cyclic ketones. However, it proved that alicyclic ketones, in contrast to aromatic and heterocyclic ketones, are considerably poorer in condensation cyclopentanone and cyclohexanone with the ethyl p-toluenesulfonate of 2-methylbenzothiazole, there were obtained the ethyl p-toluenesulfonates of 2-cyclopentylidenemethyl- and 2-cyclohexylidenemethylbenzothiazole.



These quaternary salts were condensed with the ethiodide of 2-methylmercaptobenzothiazole, obtaining 8,9-trimethylene- and 8,9-tetramethylenethiacyanines with λ_{\max} : (XIII) $n = 3,570$; (XIV) $n = 4,571$ (in m μ).



Ring closure at the 8,9 position of the polymethine chloroform • probably creates considerable steric hindrance, as a result of which the dyes we synthesized have low stability and are readily decolorized by bases. The figure shows absorption curves for 8,9-tetramethylenethiacarbocyanine (XIV), 8,10-dimethylthiacarbocyanine (II) [6], for which



there is considerable steric hindrance, and 3,3'-diethylthiacarbocyanine (III). From the figure it is evident that the steric hindrance is reflected not only in the position of the absorption maximum, but also in the form of the absorption curve. The quaternary salts (B) and (C) do not enter into condensation with the ethiodide of 2- β -acetanilidovinylbenzothiazole nor with 3-ethyl-2-formylmethylenbenzothiazoline.

EXPERIMENTAL

Indanone-1 [7], α -tetralone [8], cyclopentanone [9], *m*-nitroacetophenone [10], *o*-nitroacetophenone [11], and γ -acetylpyridine [12] were prepared by methods described in the literature.

Ethyl *p*-toluenesulfonate of 2- β -(*m*-nitrophenyl)-propenylbenzothiazole. A mixture of 6.9 g of the ethyl *p*-toluenesulfonate of 2-methylbenzothiazole, 8.2 g of *m*-nitroacetophenone, and 12 ml acetic anhydride was heated 12 hr at 155-160°. After cooling, 120 ml ether was added to the mass, and the mixture was shaken vigorously. After 3 hr the ether solution was decanted off. The dark viscous mass was again treated with 100 ml ether and then dissolved in methanol, after which the solution was diluted with water up to the appearance of turbidity, boiled with bone black, filtered, and allowed to stand until the following day. The black precipitate was filtered off, and the solution was evaporated on a steam bath. A black viscous mass was obtained, which was brought into condensation without further treatment. Weight 9 g. We were not able to separate the propenyl derivative completely from the ethiodide of 2-methylbenzothiazole by the action of potassium iodide.

Ethyl *p*-toluenesulfonate of 2- β -(*o*-nitrophenyl)-propenylbenzothiazole. A mixture of 10.4 g of the ethyl *p*-toluenesulfonate of 2-methylbenzothiazole, 20.6 g of *o*-nitroacetophenone, and 10 ml acetic anhydride was heated 16 hr at 150-155°. The treatment and purification of the reaction mass was as indicated above. Weight of the propenyl derivative 12 g (contaminated with the ethyl tosylate of 2-methylbenzothiazole).

Ethyl *p*-toluenesulfonate of 2- β -(*p*-methoxyphenyl)-propenyl-6,7-benzobenzothiazole. A mixture of 19.7 g of the ethyl *p*-toluenesulfonate of 2-methyl-6,7-benzobenzothiazole, 20 g of *p*-methoxyacetophenone, and 12 ml acetic anhydride was heated in a paraffin bath 15 hr at 165-170°. After the heating period, the mass was poured into 500 ml water and extracted twice with 150 ml portions of ether. The aqueous layer was separated off and allowed to stand 1.5 hr. The precipitated ethyl *p*-toluenesulfonate of 2- β -(*p*-methoxyphenyl)-propenyl-6,7-benzobenzothiazole was filtered off and dried. Yield 1.6 g (6%), m.p. 179° (decomp.). The aqueous solution was heated to 40°, and 10 g potassium iodide in 15 ml hot water was added. After standing 5 hr, the precipitate was filtered off and dried. Yield 5.8 g (23.8%). M.p. 200-201° (decomp.). Total yield of quaternary salts 29.8%.

Ethyl *p*-toluenesulfonate of 2- β -(*o*-methoxyphenyl)-propenyl-6,7-benzobenzothiazole. A mixture of 5.9 g of the ethyl *p*-toluenesulfonate of 2-methyl-6,7-benzobenzothiazole, 7.5 g of *o*-methoxyacetophenone, and 5 ml acetic anhydride was heated 10 hr at 155-165°, and 4 hr at 175-180°. The reaction mixture was treated first with 250 ml of ether, and then with 150 ml. The black, noncrystalline mass was extracted repeatedly with boiling water (total volume of water about 500 ml). The aqueous solution was boiled with bone black, filtered, and evaporated on a steam bath. For removing the initial quaternary salt, the viscous mass was washed three times with hot water. Each time after stirring with hot water, the mixture was allowed to stand for cooling. After the third wash, the residue in the dish crystallized. It was filtered off and dried. Yield 3.6 g (13.5%), m.p. 78°.

Ethyl *p*-toluenesulfonate of 2- β -(*p*-methoxyphenyl)-propenylbenzothiazole. A mixture of 17.2 g of the ethyl *p*-toluenesulfonate of 2-methylbenzothiazole, 15 g of *p*-methoxyacetophenone, and 15 ml acetic anhydride was boiled 6 hr. After preliminary purification (see above), the orange semicrystalline mass was mixed with ether, benzene, and then again with ether, for removal of the *p*-methoxyacetophenone. The addition of 30-35 ml water to the viscous mass gave lustrous orange tablets, which were filtered off and washed with 2-3 ml water. After adding potassium

*As in original. Possibly should be chromophore.

** Temperature of paraffin bath.

iodide to the wash waters, the propenyl derivative was not precipitated. Yield 5 g (20%), m.p. 167-168°. The product was crystallized from water, using bone black. Long, lustrous, fluffy needles of an orange color, m.p. 171-172°. λ_{\max} 389 m μ .

Found %: S 13.20, 13.11. $C_{26}H_{27}O_4NS_2$. Calculated %: S 13.30.

Ethiodide of 2- β -(α -naphthyl)-propenylbenzothiazole. A mixture of 17.4 g of the ethyl p-toluenesulfonate of 2-methylbenzothiazole and 17 g of α -acetylnaphthalene was heated 15 hr at 160-165°. The reaction mixture was transferred to a one liter Erlenmeyer flask, to which there was added 90 ml water and 150 ml ether. The mixture was agitated vigorously until the viscous mass was completely dissolved. The aqueous layer was separated from the ether and extracted again with 150 ml of ether. Then 15 g potassium iodide dissolved in 15 ml hot water was added to the aqueous solution. An oil separated out, and crystallized. On the following day the precipitate was filtered off, washed with a small quantity of water, and crystallized from methanol. Yield 3.8 g (17%). Lustrous yellow-orange tablets, m.p. 109° (decomp.).

Ethiodide of 2- β -(α -thienyl)-propenyl-4,5-benzobenzothiazole. A mixture of 3.9 g of the ethyl p-toluenesulfonate of 2-methyl-4,5-benzobenzothiazole and 6.5 g of α -acetylthiophenone was heated 12 hr at 155-160°. The reaction mass was poured into 60 ml water and 100 ml ether and then agitated vigorously until solution was complete. The aqueous layer was separated from the ether, and the ether was washed with 20 ml water. The aqueous extracts were extracted again with 100 ml ether. The aqueous layer was separated, and 10 g potassium iodide in 10 ml water was added to it. Yield 1.56 g (33%), m.p. 192°.

Ethiodide of 2-(tetralnylidene- α -methyl)-benzothiazole (Salt A). A mixture of 17.4 g of the ethyl p-toluenesulfonate of 2-methylbenzothiazole and 14.6 g of α -tetralone was heated in a paraffin bath 16 hr at 160-165°. The reaction mass was poured into a one-liter Erlenmeyer flask, and 50 ml water and 100 ml ether was added to it. After vigorous agitation, the aqueous layer was separated off, and the ether layer was extracted with 15 ml water. The combined aqueous extracts were extracted again with 100 ml ether, after which the aqueous layer was separated off and treated with 10 g potassium iodide in 15 ml hot water. The precipitate was broken up, filtered off, dried, and dissolved in 30 ml boiling methanol; the mixture was allowed to stand 3 hr. The yellow-orange crystals were filtered off and washed with a small quantity of methanol. Yield 2.9 g (13.4%), m.p. 210-211° (decomp.).

Found %: I 30.20, 30.23. $C_{20}H_{20}NSI$. Calculated %: I 29.33.

Ethyl p-toluenesulfonate of 2-cyclopentylidenemethylbenzothiazole (Salt B). A mixture of 6.9 g of the ethyl p-toluenesulfonate of 2-methylbenzothiazole, 8.4 g cyclopentanone, and 10 ml acetic anhydride was heated 12 hr at 160-165°. After the usual treatment with ether, dissolving of the residual viscous mass in methanol, dilution of the methanol solution with water until turbidity appeared, boiling the solution with bone black, and evaporating the solution on a steam bath, there was obtained a viscous, noncrystalline, dark-colored mass. Then the sulfonate was treated with a small quantity of water, and the water was separated from the viscous noncrystalline mass, which was dried on a steam bath. Yield 1.7 g (20%).

Ethyl p-toluenesulfonate of 2-cyclohexylidenemethylbenzothiazole (Salt C). A mixture of 10.4 g of the ethyl p-toluenesulfonate of 2-methylbenzothiazole, 19.6 g of cyclohexanone, and 10 ml acetic anhydride was boiled 10 hr. After cooling, 180 ml ether was added to the mixture, the mass was stirred vigorously, the ether was poured off, and the mass was washed again with 100 ml ether. After dissolving the residue in 200 ml boiling water, the solution was boiled with bone black, filtered, and evaporated on a steam bath. The noncrystalline, yellow-orange mass was mixed with 30 ml cold water, separated from the water, and dried on a steam bath. Yield 3.2 g (36%).

Ethyl p-toluenesulfonate of 2- β -anilidovinyl-5-methoxybenzothiazole. For synthesizing carbocyanines, we needed the quaternary salt of 2- β -anilidovinyl-5-methoxybenzothiazole. It was found that during the condensation of the ethyl p-toluenesulfonate of 2-methyl-5-methoxybenzothiazole with diphenylformamidine in acetic anhydride, the sole product formed is the ethyl p-toluenesulfonate of 2- β -anilidovinyl-5-methoxybenzothiazole, as was proven by synthesis of the indicated intermediate product from the ethyl p-toluenesulfonate of 2-methyl-5-methoxybenzothiazole and ethylisoformanilide, and also by analytical data.

a) A mixture of 3.79 g of the ethyl p-toluenesulfonate of 2-methyl-5-methoxybenzothiazole, 1.96 g of diphenylformamidine, and 7 ml acetic anhydride was boiled on a screen for 10 min. To the precipitate there was added 30 ml anhydrous acetone, and the crystals were filtered off, washed with acetone, methanol, and ether, and then dried. Yield 2.2 g (42%), m.p. 261-262°. After crystallization from alcohol, fine yellow needles were ob-

tained, m.p. 273-274° (decomp.). For the subsequent condensation, there was no necessity for crystallizing the product.

Found %: S 13.46, 13.40. $C_{25}H_{26}O_4N_2S_2$. Calculated %: S 13.27.

b) A mixture of 1.89 g of the ethyl p-toluenesulfonate of 2-methyl-5-methoxybenzothiazole and 0.81 g of ethylisoformanilide [13] was heated with stirring up to 155° for 5 min, and at 135-140° (paraffin bath temperature) for 1 hr. Then the precipitate was mixed thoroughly with acetone, filtered off, and washed on the filter with acetone and then with methanol to remove the thiocarbocyanine. Finally, the product was crystallized from alcohol. Yield 1.2 g (50%). Yellow needles, m.p. 273-274° (decomp.). A mixed sample with the product obtained by method "a" did not give any melting point depression.

Found %: S 13.34, 13.53. $C_{25}H_{26}O_4N_2S_2$. Calculated %: S 13.27.

Dyes

3,3'-Diethyl-9-(o-nitrophenyl)-thiocarbocyanine iodide (III). A mixture of 4.9 g of the ethyl p-toluenesulfonate of 2-β-(o-nitrophenyl)-propenylbenzothiazole and 3.3 g of the ethiodide of 2-methylmercaptobenzothiazole was dissolved in 35 ml of anhydrous alcohol. Triethylamine (1.5 ml) was added to the solution, and the mixture was boiled 35 min, and then allowed to stand until the following day. The precipitated monomethinecyanine was filtered off and washed on the filter with alcohol, and the thiocarbocyanine was precipitated with water. The viscous mass was separated from the aqueous layer, dried in air, dissolved in chloroform, and subjected to chromatography on aluminum oxide. A violet colored zone was separated, which on the aluminum oxide was partially decolorized. The violet colored zone was removed from the column and treated with alcohol, the solution was filtered, the alcohol was driven off, and the residue was crystallized from alcohol. Fine black crystals, m.p. 243-244° (decomp). Yield 0.14 g (2.2%).

3,3'-Diethyl-9-(m-nitrophenyl)-thiocarbocyanine iodide (IV). An 8 g quantity of the ethyl p-toluenesulfonate of 2-β-(m-nitrophenyl)-propenylbenzothiazole and 6.1 g of the ethyl p-toluenesulfonate of 2-methylmercaptobenzothiazole were dissolved in 50 ml of anhydrous alcohol. Triethylamine (2 ml) was added to the hot solution, and the mixture was boiled 30 min. The dye was precipitated with water; the precipitate was filtered off, washed with water, dried, dissolved in chloroform, and chromatographed on aluminum oxide. The chloroform was driven off completely from the eluate, the residue was dissolved in boiling alcohol, and the dye was precipitated by the action of an aqueous potassium iodide solution. After crystallizing from alcohol, yield 1.3 g (13%). Black crystals, m.p. 262-263° (decomp.).

3,3'-Diethyl-9-(p-methoxyphenyl)-6,7,6',7'-dibenzothiacarbocyanine bromide (VI). To a solution of 0.44 g of the ethyl p-toluenesulfonate of 2-methylmercapto-6,7-benzobenzothiazole and 0.53 g of the ethyl p-toluenesulfonate of 2-β-(p-methoxyphenyl)-propenyl-6,7-benzobenzothiazole in 5 ml anhydrous alcohol, 0.5 ml of triethylamine was added, and the mixture was boiled 35 min on a steam bath. The dye was precipitated by potassium bromide and crystallized from alcohol. Yield 0.45 g (69%). Large lustrous green tablets, m.p. 265°.

Found %: Br 12.43, 12.44. $C_{36}H_{31}ON_2S_2Br$. Calculated %: Br 12.28.

3,3'-Diethyl-9-(o-methoxyphenyl)-6,7,6',7'-dibenzothiacarbocyanine bromide (IX). A mixture of 1.7 g of the ethyl p-toluenesulfonate of 2-β-(o-methoxyphenyl)-propenyl-6,7-benzobenzothiazole and 1.4 g of the ethyl p-toluenesulfonate of 2-methylmercapto-6,7-benzobenzothiazole was dissolved in 10 ml anhydrous alcohol. Triethylamine (0.5 ml) was added to the solution, and the mixture was boiled 40 min on a steam bath. Yield 1.27 g (57%). Lustrous green crystals, m.p. 274°.

Found %: Br 12.35. $C_{36}H_{31}ON_2S_2Br$. Calculated %: Br 12.28.

3,3'-Diethyl-9-(p-hydroxyphenyl)-6,7,6',7'-dibenzothiacarbocyanine bromide (VII). A mixture of 0.2 g of the dye (VI) and 2 ml hydrobromic acid (d. 1.76, 66%) was heated 7 hr at 150-155° in a sealed tube. The tube was opened, the contents were added to 70 ml water, and the precipitate was filtered off, washed with water, dried, and crystallized from alcohol. Yield 0.14 g (73%). Green crystals, m.p. 308° (decomp.).

Found %: S 10.10, 10.21. $C_{35}H_{29}ON_2S_2Br$. Calculated %: S 10.00.

3,3'-Diethyl-9-(o-hydroxyphenyl)-6,7,6',7'-dibenzothiacarbocyanine bromide (X). A mixture of 0.15 g of the dye (IX) and 1.5 ml hydrobromic acid (d. 1.76, 66%) was heated 7 hr at 150-155° in a sealed tube. Yield 0.08 g (57%). Black crystals, m.p. 277°.

Found %: S 10.46, 10.47. $C_{35}H_{29}ON_2S_2Br$. Calculated %: S 10.00.

3,3'-Diethyl-9-phenyl-8-o-dimethylenethiacarbocyanine perchlorate (XII). A mixture of 0.86 g of the ethiodide of 2-(tetralinylidene- α -methyl)-benzothiazole, 0.66 g of the ethiodide of 2-methylmercaptobenzothiazole, 1 g anhydrous sodium acetate, and 10 ml anhydrous alcohol was boiled 45 min on a steam bath. The reaction mixture was poured into a hot aqueous solution of potassium iodide. On the following day the water was separated from the dark viscous mass, and the latter was washed twice with water and dried in air, then dissolved in chloroform and subjected to chromatography on aluminum oxide. Elution with chloroform was continued up to the time when the blue zone started to come off; this zone was removed mechanically from the column, and the dye was removed from the adsorbent with methanol. After filtration, the methanol was driven off completely, the residue was dissolved in a minimum quantity of methanol, and to the hot solution there was added 0.5 g sodium perchlorate in 5 ml hot water, after which the solution was allowed to stand for crystallization. On the following day the precipitate of the dye was filtered off, washed with warm water and with ether, and dried. Yield 0.14 g (10%). Black crystals, m.p. 176-177° (decomp.).

Found %: S 11.21, 11.30. $C_{29}H_{27}O_4N_2S_2Cl$. Calculated %: S 11.29.

3,3'-Diethyl-8,9-trimethylenethiacarbocyanine perchlorate (XIII). A mixture of 2.07 g of the ethyl p-toluenesulfonate of 2-cyclopentylidenemethylbenzothiazole, 1.68 g of the ethiodide of 2-methylmercaptobenzothiazole, 2 g sodium acetate, and 25 ml anhydrous alcohol was boiled 25 min. The sodium acetate was filtered off and washed with methanol, and the dye was precipitated with sodium perchlorate. The viscous mass was stirred with 2 ml acetone, and the precipitate was filtered off and crystallized twice from alcohol. Yield 0.4 g (18%). Fine dark-green crystals, m.p. 218° (decomp.).

Found %: Cl 7.25, 7.35. $C_{24}H_{25}O_4N_2S_2Cl$. Calculated %: Cl 7.03.

3,3'-Diethyl-8,9-tetramethylenethiacarbocyanine perchlorate (XIV). A mixture of 4.29 g of the ethyl p-toluenesulfonate of 2-cyclohexylidenemethylbenzothiazole and 3.37 g of the ethiodide of 2-methylmercaptobenzothiazole was dissolved in 50 ml anhydrous alcohol. Anhydrous sodium acetate (4 g) was added to the solution, and the mixture was boiled 35 min. Yield 0.9 g (19%). Large lustrous tablets, with a bronze luster, m.p. 222°.

Found %: Cl 6.98, 7.20. $C_{25}H_{27}O_4N_2S_2Cl$. Calculated %: Cl 6.84.

SUMMARY

1. A number of quaternary salts of β -substituted 2-propenylbenzothiazoles have been obtained by the condensation of quaternary salts of substituted 2-methylbenzothiazoles with aromatic and alicyclic ketones.
2. From these quaternary salts and the ethiodides of 2-methylmercaptobenzothiazole and 2- β -acetanilidovinylbenzothiazole, thiacyanines and thiadicyanines have been obtained, and their optical properties have been studied.

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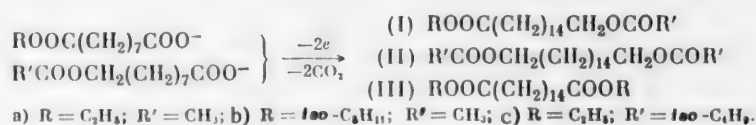
PREPARATION OF 1-HYDROXYHEXADECANOIC ACID
BY A "CROSSED" ELECTROCONDENSATION METHOD
III. ELECTROCONDENSATION OF MONOESTERS OF AZELAIC ACID
WITH ACYL DERIVATIVES OF 9-HYDROXYNONANOIC ACID

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Monoesters of azelaic and acyl derivatives of 9-hydroxynonanoic acids are starting compounds for preparing 16-hydroxyhexadecanoic acid by a "crossed" electrocondensation method. The electrosynthesis is carried out under conditions we developed for preparing 15-hydroxypentadecanoic acid [1]. Compounds (I, II, III) which are obtained by reaction of the $\text{ROOC}(\text{CH}_2)_7\text{COO}^-$ and $\text{R}'\text{COOCH}_2(\text{CH}_2)_7\text{COO}^-$ ions according to the following general scheme are the main reaction products.



Separation of (I) of free 16-hydroxyhexadecanoic acid (after saponification of the mixture of reaction products) in the case when the starting materials were ethyl azelate and 9-acetoxynonanoic acid ($\text{R} = \text{C}_2\text{H}_5$ and $\text{R}' = \text{CH}_3$) proved to be very difficult. Better results were obtained in this case by a method based on different solubilities of the potassium salts [2] of 16-hydroxyhexadecanoic acid and hexadecane dicarboxylate-1,16 obtained by saponifying compounds (I and III) in hot ethanol. Hexadecanediol-1,16 formed by saponifying (II) is easily separated from the salt mixture by extraction with organic solvents. The yield of 16-hydroxyhexadecanoic acid is 16-17% in this case (based on 9-acetoxynonanoic acid used).

In order to avoid this rather laborious separation method and to allow separation of (I, II, and III) by vacuum distillation, we conducted experiments in electrocondensation of azelaic esters and acyl derivatives of 9-hydroxynonanoic acid in which the size of R and R' radicals differed considerably. This permitted preparing (I, II, and III) with markedly greater differences in molecular weight and boiling points. With this goal we carried out experiments in electrocondensation between monoisoamylazelate and 9-acetoxynonanoic acid ($\text{R} = \text{iso-C}_5\text{H}_{11}$ and $\text{R}' = \text{CH}_3$) and monoethyl azelate with 9-iso-valeroxynonanoic acid ($\text{R} = \text{C}_2\text{H}_5$ and $\text{R}' = \text{iso-C}_4\text{H}_9$).

In contrast to the experiments described earlier [1], these were carried out with a larger quantity of water in the electrolyte (13 moles instead of 8.2 per mole of starting substance) which was a necessary condition for obtaining a homogeneous solution. Moreover, alcohol (50-60 ml per 1 mole of starting substance) was added to the electrolyte at the beginning of electrolysis to suppress the strong foaming. All other conditions for carrying out the electrocondensation process were the same as described in experimental variant "a".

Satisfactory results in separating the reaction products were obtained only for mixtures (Iv), (IIv), and (IIIv). During distillation through a laboratory fractionating column with an efficiency of about 10 theoretical plates at a residual pressure of 0.9-0.6 mm ethyl 16-hydroxyhexadecanoate was separated without admixed hexadecane-1,16 diester. The yield was 15-17%, based on 9-isovaleroxynonanoic acid used.

The yield of 16-hydroxyhexadecanoic acid by following electrocondensation variant "b" was 7-12% (separation was by potassium salts). It should be mentioned that in this variation there is considerably greater formation (nearly double) of hexadecane-1,16 diester (III) than with variants "a" or "v".

EXPERIMENTAL

I. Preparation of Substances Used for Electrocondensation

1. 9-Acetoxy-nonanoic acid. To a solution of 9-hydroxy-nonanoic acid (m.p. 44°, acid number* 296) in 100 g of acetic anhydride was added gradually 25 g of acetylating mixture (10% solution of phosphoric acid in acetic anhydride). By distillation of the reaction product 69.7 g (54.9%) of 9-acetoxy-nonanoic acid was obtained.

B. p. 172-174° (5 mm); n_D^{20} 1.4391; acid number 257.6; ester number 257.3. Calculated: $KCh = \bar{E}Ch$ 259.2. Literature data [3]; b.p. 192-193° (10 mm).

2. Monoisoamyl azelate. A mixture consisting of 204 g of azeleic acid, 200 g of diisoamyl azelate,** 100 g of isoamyl alcohol, and 500 ml of 20% sulfuric acid solution was heated 6 hr at 100-102°. Azelaic acid (83 g) not going into reaction was filtered off; the oily layer formed by the reaction was washed with soda solution. In this way 114 g of diisoamyl ester was separated. By fractionating monoisoamyl ester separated from the soda washes by acidification 155 g of product was obtained. The yield of monoisoamyl azelate was 55.4% based on azelaic acid reacting.

B. p. 164-165° (2 mm); d_4^{20} 0.9860, n_D^{20} 1.4473, MR_D 70.04; calculated 70.04.

Found %: C 65.24, 65.30; H 9.65, 9.81; acid number 216.2; ester number 217.0. $C_{14}H_{26}O_4$. Calculated %: C 65.08; H 10.14; $KCh = \bar{E}Ch$ 217.0.

3. 9-Isovaleroxynonanoic acid. To a mixture of 100 g of 9-hydroxy-nonanoic acid and 400 ml of benzene at 50-55° added 143.1 g of isovaleroyl chloride, after which the reaction mixture was heated for 1 hr more. The residue after distillation of the benzene was fractionated in vacuum. The yield of 9-isovaleroxynonanoic acid was 58.7 g.

B. p. 171-172° (2 mm); d_4^{20} 0.9827, n_D^{20} 1.4470, MR_D 70.25; calculated 70.04.

Found %: C 64.70, 64.99; H 10.17, 9.97; acid number 218.5; ester number 216.6. $C_{14}H_{26}O_4$. Calculated %: C 65.08; H 10.14; $KCh = \bar{E}Ch$ 217.5.

II. Electrolytic Condensation

Experimental data for variants "a" and "v" which differ in the method of separating the product mixture and in some steps of the electrolytic condensation process are given. The properties of the substances used are given above.

1. Electrolytic condensation of monoethyl azelate and 9-acetoxy-nonanoic acid. Into a steel electrolyzer, the wall of which serves as cathode, equipped with a thermometer, reflux condenser, and platinum anode was charged the electrolyte containing 110 g of 9-acetoxy-nonanoic acid and 330 g of monoethyl azelate neutralized with 122 g of potash in 304 ml of water. The process was carried out at a current density of 0.4 A/cm² at the anode, a voltage of 14-18 V, 40-45°, current of 13-14 A and was discontinued after passage of 180 A-hr. A low-boiling substance (52.4 g) was steam-distilled from the reaction products, but the residue (254.4 g) was distilled in vacuum. A fraction, consisting of a mixture of (Ia), (IIa) and (IIIa), was collected at 198-225° (6 mm) and weighed 117.2 g. The distilled product (117.2 g) was boiled with 900 ml of alcoholic potassium hydroxide (45 g KOH) and the reaction mixture was filtered at 60-65°. The dipotassium salt of hexadecane-1,16 diacid remained as residue; the potassium 16-hydroxyhexadecanoate and hexadecanediol-1,16 were in the filtrate. After extracting hexadecanediol and converting the salt to acid hexadecane-1,16 diacid weighing 37.4 g and melting at 121.5° (literature [4]: m.p. 124.2°), acid number 384.8, calculated 391.6; hexadecanediol-1,16 (22.4 g) m.p. 86-88°, % OH, 12.2 (literature [4]: m.p. 88.5-91.4°), calculated % OH, 13.2; and 16-hydroxyhexadecanoic acid (22.5 g) melting at 87-88°, acid number 219.9, % OH, 6.0 (literature [3]: m.p. 95°); calculated acid number 206.3, % OH, 6.2 were obtained. The yield of 16-hydroxyhexadecanoic acid was 17% based on 9-acetoxy-nonanoic acid used.

2. Electrolytic condensation of monoethyl azelate with 9-isovaleroxynonanoic acid. A solution containing 90 g of 9-isovaleroxynonanoic acid, 226 g of monoethyl azelate, and 84 g of K₂CO₃ in 216 ml of water was elec-

* Here and further on, KCh = acid number, $\bar{E}Ch$ = ester number.

** Diisoamyl azelate obtained by esterification of azelaic acid with isoamyl alcohol in aqueous sulfuric acid solution has the following constants: b.p. 161-162° (2 mm); d_4^{20} 0.9295, n_D^{20} 1.4415, MR_D 93.41; calculated 93.25.

Found %: C 69.67, 69.51; H 10.84, 10.89; acid number 340.8. $C_{19}H_{36}O_4$. Calculated %: C 69.47; H 11.05; ester number 341.4.

trolyzed under the conditions described above. To eliminate foaming during electrolysis 25 ml of alcohol was added. A current of 92 A-hr was passed. The residue (206 g) after distillation of low-boiling compounds (42.4 g) from the electrolysis products was distilled through a column of 10 theoretical plates efficiency at a residual pressure of 0.9-0.6 mm. The fraction collected to 185° (0.6 mm) contained no ester of 16-hydroxydodecanoic acid. The higher boiling fractions and residue after distillation contained the hydroxyacid ester and diol. Upon saponification of the fractions boiling at 185-195° (0.6 mm) and 198-202° (0.6 mm) and the residue from vacuum distillation 15.8 g of 16-hydroxyhexadecanoic acid melting at 84-86°, % OH 6.0, acid number 219.2 was separated. The yield of 16-hydroxyhexadecanoic acid was 16.8% based on 9-isovaleroxynonanoic acid.

SUMMARY

Electrolytic condensation of monoethyl and monoisoamyl azelate with 9-acetoxynonanoic acid, and also of monoethyl azelate with 9-isovaleroxynonanoic acid was accomplished. The yield of 16-hydroxyhexadecanoic acid was 17% based on 9-acetoxynonanoic acid.

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FLUORENE CHEMISTRY

II. FRIEDEL-CRAFTS ACYLATION OF FLUORENE

WITH MALEIC ANHYDRIDE

A. E. Kretov and V. V. Lutvinov

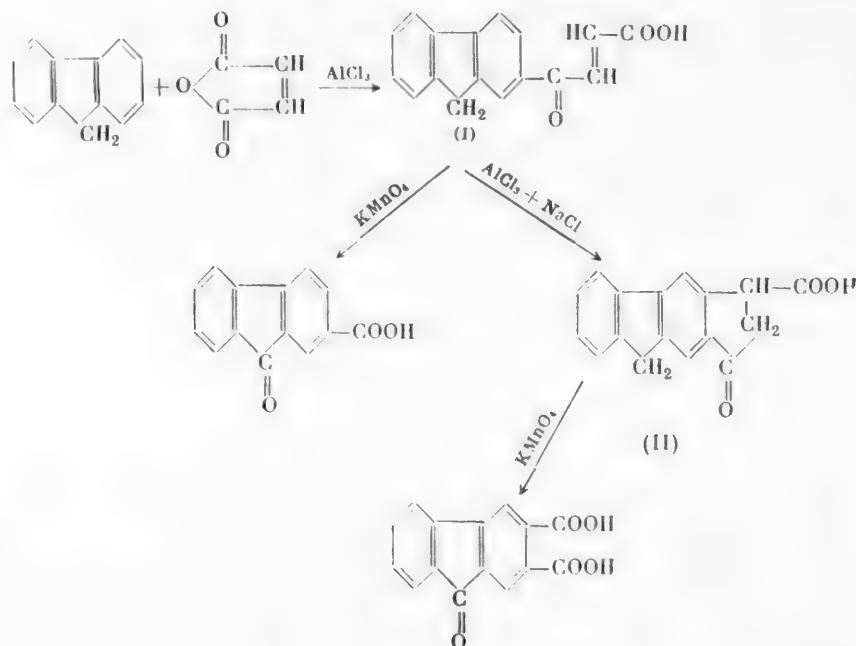
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

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Original article submitted September 9, 1960

Aromatic hydrocarbons and maleic anhydride form β -aroalacrylic acids having the trans configuration in the presence of aluminum chloride [1-3]. Acylation of polycyclic hydrocarbons by maleic anhydride has not been studied thoroughly. The acylation of naphthalene, phenanthrene, and acenaphthene and of fluorene with itaconic anhydride have been described [4-6]. Solid aluminum chloride or an excess of it nearly always shows a harmful effect on the yield of acylation product. In order to avoid this, a solution of a maleic anhydride-aluminum chloride complex in 1 : 2 molar ratio in methylene chloride or dichloroethane was prepared and it was poured into a solution of hydrocarbon in the same solvent [7]. Isomerization of β -aroalacrylic acids by heating with a fused mixture of aluminum and sodium chlorides led to formation of cyclic products [4].

Since β -2-fluorenylacrylic acid (I) has several reactive centers and has very wide synthetic potentialities, we studied the acylation of fluorene with maleic anhydride in the presence of aluminum chloride. β -2-Fluorenylacrylic acid, the structure of which was demonstrated by oxidation to the known fluorene-2-carboxylic acid, was formed as a result of the reaction. The acid obtained (I) decolorized bromine water and readily added hydrogen chloride or hydrogen bromide to form the corresponding saturated acids. By heating β -2-fluorenylacrylic acid in a fused mixture of aluminum and sodium chlorides it isomerized into 2,3-cyclopentanofluorene-1'-one-3'-carboxylic acid (II), the structure of which was proved by oxidation with potassium permanganate to previously described fluorenone-2,3-dicarboxylic acid. The reactions we studied can be represented by the following scheme:



EXPERIMENTAL

Preparation of β -2-fluorenolacrylic acid. To a solution of 19.6 g of maleic anhydride in 120 ml of dichloroethane was added 56 g of pulverized aluminum chloride over a period of 20 min with stirring; this was stirred 30 min more and the solution was slowly decanted (with little residual solid aluminum chloride) into a flask containing a solution of 33.2 g of fluorene in 100 ml of dichloroethane. The reaction mixture was stirred at room temperature for 3 hr and left overnight, after which it was poured into a flask containing 300 g of ice and 50 ml of concentrated hydrochloric acid. The residue was removed by filtration and washed with dilute hydrochloric acid. The yield of acid (I) was 85%. M.p. 200-201° (decomp.) from glacial CH_3COOH .

Found %: C 77.30, 77.34; H 4.61, 4.65. $\text{C}_{17}\text{H}_{12}\text{O}_3$. Calculated %: C 77.25; H 4.54.

Preparation of β -2-fluorenolbromopropionic acid. To a suspension of 2.5 g of β -2-fluorenolacrylic acid in 125 ml of glacial acetic acid hydrogen bromide was added until complete decolorization of starting material occurred. β -2-Fluorenolbromopropionic acid was formed in quantitative yield and melted at 170-171° (decomp.).

Found %: Br 23.22, 23.18. $\text{C}_{17}\text{H}_{13}\text{O}_3\text{Br}$. Calculated %: Br 23.15.

β -2-Fluorenylchloropropionic acid melting at 192-193° (decomp.) was prepared similarly.

Found %: Cl 11.72, 11.63. $\text{C}_{17}\text{H}_{13}\text{O}_3\text{Cl}$. Calculated %: Cl 11.78.

Oxidation of β -2-fluorenolacrylic acid. To a flask, containing 180 ml of 2% sodium hydroxide and 3.5 g of β -2-fluorenolacrylic acid was added in small portions over a duration of 1 hr 12.8 g of potassium permanganate; the reaction vessel was warmed on a water bath at 80-90° for 2 hr more. At the end of the reaction the manganese dioxide was removed by filtration and washed with a 2% sodium hydroxide solution. The filtrate was acidified; the fluorenone-2-carboxylic acid which precipitated was removed by filtration and crystallized from acetic acid, m.p. 327-330° (literature [8]: m.p. 330°). For more positive identification the acid was converted to its methyl ester melting at 180-181° (literature [8]: m.p. 181°).

Isomerization of β -2-fluorenolacrylic acid. β -2-Fluorenolacrylic acid (9 g) was added in small portions to a fused mixture of 90 g of aluminum chloride and 13.5 g of sodium chloride; the reaction mixture was heated for 45 min at 120-125° and then added to a flask with 300 g of ice and 50 ml of concentrated hydrochloric acid. The residue was filtered off, washed with dilute hydrochloric acid, and then water; it was dissolved in 2% sodium bicarbonate and filtered; the filtrate was boiled with active charcoal and then acidified; the precipitated residue of 2,3-cyclopentanofluorene-1'-one-3'-carboxylic acid was filtered off and again purified through the sodium salt. M.p. 208-210° (decomp.).

Found %: C 77.63, 77.58; H 4.92, 4.83. $\text{C}_{17}\text{H}_{12}\text{O}_3$. Calculated %: C 77.25; H 4.54.

Preparation of methyl 2,3-cyclopentanofluorene-1'-one-3'-carboxylate. The acid (1.3 g) and 60 ml of anhydrous methyl alcohol were charged into a flask; a strong stream of dry hydrogen chloride was introduced for 20 min duration, after which the flask was cooled to 0°; the reaction mixture was thus saturated with hydrogen chloride and left for 2 hr. Then the contents of the flask were added to a beaker of ice and crystalline sodium carbonate; the residue was filtered off, washed with soda solution, then water, and crystallized from pyridine and toluene. M.p. 138-140° (decomp.).

Found %: C 77.85, 77.92; H 4.79, 4.86. $\text{C}_{18}\text{H}_{14}\text{O}_3$. Calculated %: C 77.69; H 5.03.

Oxidation of 2,3-cyclopentanofluorene-1'-one-3'-carboxylic acid. To a flask containing 300 ml of 2% sodium hydroxide solution and 5 g of acid, immersed in a water bath at 80-90°, was added in small portions over 2 hr 26 g of potassium permanganate, after which heating was continued 2 hr more. The residual manganese dioxide was filtered off and washed with caustic; the filtrate was acidified and the precipitate was recrystallized from glacial acetic acid. The fluorenone-2,3-dicarboxylic acid isolated had a wide melting range (246-272°; literature [9]: m.p. 250-275°) since it is easily converted to the anhydride. For more positive identification the dimethyl ester, which melted at 132-133° (literature [9]: m.p. 131-133°) was synthesized; it did not give melting point depression with a pure preparation.

SUMMARY

1. β -2-Fluorenolacrylic acid was prepared and its structure demonstrated by oxidation to fluorenone-2-carboxylic acid.

2. β -2-Fluorenylbromopropionic and β -2-fluorenylchloropropionic acids were obtained.
3. An isomerization product of β -2-fluorenylacrylic acid was prepared and its structure was demonstrated.
4. Derivatives of fluorenone-2-carboxylic and fluorenone-2,3-dicarboxylic acids as well as of 2,3-cyclopentanofluorene-1'-one-3'-carboxylic acid were prepared.

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ASYMMETRIC TERTIARY ARSINES

II. p- TOLYLETHYLALKYLARSINES AND THEIR DERIVATIVES

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In the previous paper [1] we described a series of phenylethylalkylarsines and some of their properties. Continuing studies in this direction, we carried out new syntheses of aliphatic-aromatic arsines. Synthesis of the original halosubstituted secondary arsine was accomplished by reaction of tetraethyllead with p-tolyldichloroarsine at elevated temperature (about 120°).



p-Tolyethylchloroarsine was thus isolated in 88.3% yield.

Various asymmetric arsines were obtained by reaction of p-tolyethylchloroarsine with solutions of Grignard reagents prepared from the corresponding haloalkanes. Some data concerning them is presented in Table 1.

p-Tolyldiethylarsine was first synthesized [2] by another method, but besides a boiling point at 250° no other data were presented. We previously synthesized ethyl-n-propyl-p-tolylarsine by another method [3].

All of the trivalent arsines we obtained were colorless, easily mobile liquids with clinging odors. They are soluble in ether, alcohol, benzene, and other organic solvents but are insoluble in water.

The trivalent arsines isolated react with cuprous bromide to yield complex salts. Thus, a complex melting at 118-119° was obtained from ethyl-n-propyl-p-tolylarsine.

As is seen from Table 1, the atomic refraction of the aliphatic-aromatic arsines synthesized is in the range 12.04, i.e., complete agreement is found with the atomic refraction of phenylethylalkylarsines previously prepared.

Crystalline arsonium compounds, some of the properties of which are given in Table 2, were obtained by the reaction of allyl bromide or benzyl bromide with tertiary arsines.

Quaternary asymmetric arsonium compounds are white crystalline substances soluble in alcohol, acetone, water and insoluble in ether.

EXPERIMENTAL

Preparation of p-tolyethylchloroarsine. In a four-necked flask equipped with stirring, dropping funnel, reflux condenser, and thermometer with continuous nitrogen blanketing was charged 150 g of p-tolyldichloroarsine which was heated in an oil bath to 110-120° (bath temperature 120-145°). Then 68.0 g of tetraethyllead was added through the dropping funnel to the warm p-tolyldichloroarsine. Turbidity and appearance of a white residue indicated the beginning of the reaction. The reaction was continued until ethyl chloride no longer was evolved through a calcium chloride tube. A fraction boiling at 126-127° (11 mm) weighing 129 g (88.3%) was obtained by vacuum distillation.

Found %: As 32.25; Cl 15.58. $\text{C}_9\text{H}_{12}\text{ClAs}$. Calculated %: As 32.48; Cl 15.43.

p-Tolyethylchloroarsine is a transparent liquid, d_4^{20} 1.3231, n_D^{20} 1.5840.

Preparation of methylethyl-p-tolylarsine. To an ethereal solution of methyl magnesium iodide obtained from 1.55 g of magnesium and 9.1 g of methyl iodide in 50 ml of ether was cautiously added drop by drop 15 g of p-tolyethylchloroarsine under a stream of inert gas with external cooling. Then the reaction mixture was left at room temperature for some hours. After decomposition with a solution of ammonium chloride the ether layer was separated,

TABLE 1

Formula	Boiling point (10 mm)	d_4^{20}	n_D^{20}	% As		$M R_D$	$A R_D$	Yield (in %)
				calc.	found			
$\begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-CH_3$	102–103°	1.1671	1.5565	35.64	35.43	57.90	12.02	81.8
$\begin{matrix} C_3H_7 \\ C_3H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_2H_5$	109–110	1.1418	1.5504	33.46	33.38	62.52	12.02	84.2
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_7H_7-H.$	122–123	1.1190	1.5445	31.45	31.15	67.21	12.08	71.3
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_6H_5-H.$	137–138	1.0978	1.5374	29.70	29.51	71.73	11.97	84.7
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_6H_{11}-H.$	152–153	1.0868	1.5359	28.20	27.97	76.29	11.99	87.5
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_6H_{13}-H.$	164–165	1.0673	1.5286	26.70	26.58	81.04	12.08	59.6
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_7H_{11}-H.$	132 (1)	1.0510	1.5235	25.45	25.23	85.51	12.04	58.1
$\begin{matrix} C_7H_7 \\ C_7H_7 \end{matrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As-C_8H_{17}-H.$	147 (1)	1.0325	1.5180	24.29	24.06	90.36	12.14	61.8

TABLE 2

Formula	Melting point	Empirical formula	% As		% Br		Yield (in %)
			calc.	found	calc.	found	
$\begin{bmatrix} C_7H_7 \\ C_7H_7 \end{bmatrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As \begin{bmatrix} C_6H_5 \\ C_2H_5 \end{bmatrix} Br$	78–79°	$C_{15}H_{24}BrAs$	20.85	20.81	22.27	22.13	73.4
$\begin{bmatrix} C_7H_7 \\ C_7H_7 \end{bmatrix} \begin{matrix} \diagup \\ \diagdown \end{matrix} As \begin{bmatrix} CH_3 \\ C_7H_7 \end{bmatrix} Br$	110–111	$C_{17}H_{22}BrAs$	19.65	19.23	20.96	20.77	61.7

washed with water, and dried over calcium chloride. After removal of solvent the residual liquid was distilled under vacuum. B.p. 122–123° (10 mm). Yield 10.6 g (81.8%).

Found %: As 35.43. $C_{10}H_{15}As$. Calculated %: As 35.64.

Methylethyl-p-tolylarsine is a colorless liquid with an unpleasant odor which is soluble in ether, alcohol, benzene, and other organic solvents.

Other arsines were obtained in a manner like that described above; their properties are presented in Table 1.

Preparation of Ethyl-n-Propylallyl-p-Tolylarsonium Bromide

To 3.0 g of ethyl-n-propyl-p-tolylarsine in a tube was added 1.62 g of allyl bromide. The tube was sealed. After heating for 6 hr at 130° 3.43 g of a crystalline substance melting at 78–79° was separated.

Found %: As 20.81; Br 22.13. $C_{15}H_{24}BrAs$. Calculated %: As 20.85; Br 22.27.

Ethyl-n-propyl-p-tolylallylarsonium bromide is a crystalline substance soluble in alcohol, acetone, ethyl acetate, and water.

Methylethyl-p-tolylbenzylarsonium bromide was synthesized by the method described above.

Preparation of a complex with cuprous bromide. To 1.5 g of ethyl-n-propyl-p-tolylarsine was added 0.95 g of cuprous bromide. The tube was sealed and warmed slightly. Upon cooling 2.1 g of a crystalline substance melting at 118-119° was obtained.

Found %: As 19.48; Br 21.08. $C_{22}H_{29}BrCu$. Calculated %: As 19.60; Br 20.91.

SUMMARY

1. A convenient method for preparing ethyl-p-tolylchloroarsine was developed.
2. Some new tertiary arsines were synthesized and their properties were studied.

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STUDY OF THE REACTION OF PROPYLENE OXIDE WITH CYANAMIDE. II

A. E. Kretov and I. S. Matveev

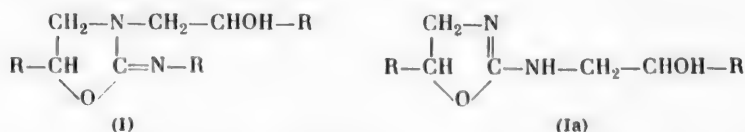
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Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,
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The syntheses of monoalkylolcyanamides [1-3] and dialkylolcyanamides [4] are described in the literature. Conditions for the synthesis of cyclic compounds - 2-iminooxazolidine and its derivatives from alkylene oxides as well as the corresponding chlorohydrins and the appropriate cyanamide salt - were discovered by Fromm and collaborators [5-8].

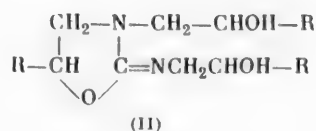
We investigated the reaction of cyanamide with propylene oxide (taken in excess) in a steel autoclave with stirring under pressure at comparatively low temperatures in the presence of added caustic acting as catalyst (alcoholic solution of caustic or calcium hydroxide) both without solvent and in benzene. In all of these cases complex mixtures, not individual substances, in the form of viscous yellow liquids were formed. By fractional distillation separation of the product mixture was accomplished, and the composition of the mixture was determined using absorption chromatography to separate the substances. The individuality and purity of the separated substances was verified by two or three repetitions of the passage over the chromatography column.

Study of the reaction products begun with the fraction simplest in composition. The analyses obtained showed that compound (I) was formed from one cyanamide molecule and two propylene oxide molecules. Its structure was determined by studying its methylation product, which contained one methoxyl group. Therefore, the starting material had a cyclic structure. In the opposite case it must contain two hydroxyl groups, and two methoxy groups after methylation. The absence of a nitrile group in the substance is shown by its failure to give an amide [9] or thioamide [10]; this also supports its cyclic structure. The cyclic structure of the given substance was also demonstrated by hydrolysis of the methoxy derivative with ethanolic potassium hydroxide and formation of β -methoxy- β' -hydroxydipropylamine, methylamine, and gaseous carbon dioxide. These products correspond to an imine form [11] of compound (I).

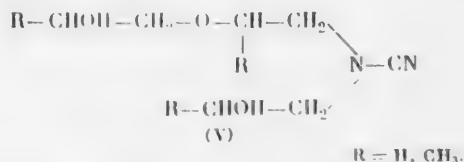
If this compound had the amine form (Ia), then β -methoxypropylamine, β -hydroxypropylamine, and gaseous carbon dioxide would be obtained by hydrolysis.



Analyses showed that the second of the substances obtained was formed from one cyanamide molecule and three propylene oxide molecules. The question of the structure of this substance was also clearly answered by studying hydrolysis products from its methylated derivative and ethanolic potassium hydroxide, as a result of which β -methoxy- β' -hydroxydipropylamine, β -methoxypropylamine, and carbon dioxide gas were obtained; this corresponds to imine form (II).

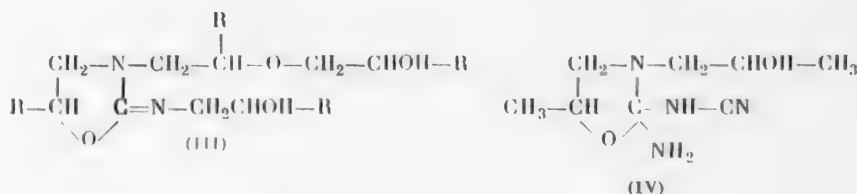


Thus the possibility of forming an amine form by hydrolysis of which β, β' -dimethoxydipropylamine, β -hydroxypropylamine and carbon dioxide would be obtained was excluded. The possibility of forming an aliphatic compound (V) was excluded since this compound does not give a reaction for the nitrile group or form 2,9-dimethoxy-4-oxa-5-methyl-7-azadecane and ammonia on hydrolysis.



Analytical data showed that the third of the substances (III) was formed from one cyanamide molecule and four propylene oxide molecules and had an imino form. By hydrolyzing its methylation product with ethanolic solution 2-methoxy-9-hydroxy-4-oxa-5-methyl-7-azadecane, β -methoxypropylamine and gaseous carbon dioxide were obtained.

The analyses obtained permit the supposition that the fourth substance was formed from one dicyandiamide molecule and two propylene oxide molecules and is 2-amino-2-cyanamido-3- β -hydroxypropyl-5-methyloxazolidine-2,3 (IV).



This substance was not studied more closely.

All the compounds were readily soluble in water, methanol, dioxane, acetone, and pyridine, but poorly soluble in benzene. They were nearly insoluble in ether; compound (III) was soluble in petroleum ether, and (IV) was insoluble in chloroform. Compounds (II) and (III) were distilled molecularly at $8 \cdot 10^{-4}$ mm: (II) at 80-86° in a glycerine bath in the form of a viscous yellow liquid, (III) at 90-94°. Compounds (I) and (IV) were not distillable under these conditions and gradually changed their composition.

EXPERIMENTAL

A mixture of 0.369 g-moles of cyanamide, 0.869 g-moles of propylene oxide and 50 mg of calcium hydroxide was placed in an autoclave and after careful mixing was heated for 3 hr at 65-75°. When the required temperature was reached in the autoclave mixing was carried out for 3-5 min out of every 30-40 min; thus heating was regulated so that rapid rises in temperature or pressure did not occur in the autoclave. The mixture obtained was a viscous yellow liquid. Temperature exhibited a decided influence on the reaction course. At 45-50° the reaction did not go even in 6 hr. At 55-65° the reaction did not go to completion. Under these conditions the yield of fraction (I) was 45-47%, (II) 28-30%, (III) 0.7-1%. There was 18-20% unreacted dicyanamide. At 65-75° the reaction went to completion, but the amount of (I) decreased to 30% while (II) increased to 43-45%. The yield of (III) was 2-3% and (IV) 20%. If the reaction was carried out in benzene the yield of products was slightly less.

Separation of the reaction products. To a separatory funnel containing 11 g of reaction mixture was added 25 ml of chloroform, which was carefully shaken and left for 1 hr. The chloroform-soluble portion was 65% of the mixture taken; the remaining part was insoluble and floated on the surface. The chloroform solution was distilled to 3/4 its volume and introduced on a chromatographic column of silica gel type ASK 28-50 and washed with 100 ml of petroleum ether, after distillation of which 0.4 g of compound (III) was obtained.

n_D^{20} 1.4840, d_4^{20} 1.0986, M_R 71.53; calc. 72.05.

Found %: N 10.07; OH 11.76. Equiv. 276. $C_8H_{26}O_4N_2$. Calculated %: N 10.22; OH 12.41. Equiv. 274.

Compound (II) (4.8 g) was eluted with 100 ml of chloroform.

n_D^{29} 1.4750, d_4^{29} 1.1340, MR_D 54.42; calc. 54.65.

Found %: N 12.88; OH 16.17. Equiv. 216. $C_{10}H_{20}O_3N_2$. Calculated %: N 12.96; OH 15.74. Equiv. 216.

The chloroform-insoluble mixture was dissolved in dioxane and passed through the same column. Compound (I) (3.6 g) was eluted with dioxane; this was passed over a starch column as a dioxane solution for further purification and was eluted with the same solvent.

n_D^{20} 1.4889, d_4^{20} 1.0200, MR_D 44.68; calc. 43.68.

Found %: N 17.93; H_{act} 1.18. Equiv. 165. $C_7H_{14}O_2N_2$. Calculated %: N 17.70; H_{act} 1.26. Equiv. 158.

Substance (IV) (2.2 g) was eluted from the silica gel column with methanol.

n_D^{20} 1.5230, d_4^{20} 1.1935, MR_D 51.00; calc. 52.52.

Found %: N 28.30. Equiv. 201. $C_8H_{16}O_2N_4$. Calculated %: N 28.10. Equiv. 199.

Complete elution of the different fractions was determined by changing refractive indices as well as by changes in the solvent color.

Methylation reaction. In a flask with stirrer was placed 0.1 g-mole of (I, II, III) and 0.22 g-mole of dimethyl sulfate. The mixture was heated for 3 hr on a boiling water bath. After cooling the reaction mixture the unreacted material was extracted with chloroform, and the remaining mixture was dissolved in acetone and passed over a silica gel chromatography column. The ethers obtained along with salts of methylsulfuric acid were viscous brown liquids and were washed with acetone. The methylsulfuric acid was titrated with 0.5 N caustic solution and steam distilled, but the residual mass was dissolved in ethanol and filtered from potassium methyl sulfate. After distilling the methanol the methylation products obtained were the indicated compounds in the form of viscous liquids.

(I) Found %: N 15.10; OCH_3 15.75. $C_9H_{18}O_2N_2$. Calculated %: N 15.05; OCH_3 16.6.

(II) Found %: N 11.43; OCH_3 24.93. $C_{12}H_{24}O_3N_2$. Calculated %: N 11.47; OCH_3 25.41.

(III) Found %: N 9.19; OCH_3 19.5. $C_{15}H_{30}O_4N_2$. Calculated %: N 9.27; OCH_3 20.52.

Hydrolysis of the ethers. In a flask with a reflux condenser was charged 0.1 g-mole of the ether and 460 ml of 2.5% ethanolic potassium hydroxide solution. The mixture was heated at 70-75° for 3 hr. The solvent was distilled from the reaction mixture, after which the amines were extracted from the residual mixture in the flask with anhydrous ethanol. The solution was neutralized with carbon dioxide gas; potassium carbonate was filtered off, and ethanol was distilled from the filtrate, leaving a mixture of aminoalcohols as a residue which was separated by vacuum distillation. β -Methoxypropylamine was distilled at 100-105° (7-9 mm) as a mobile yellow liquid.

Found %: N 15.80; OCH_3 33.79. $C_4H_{11}ON$. Calculated %: N 15.72; OCH_3 34.82.

β -Methoxy- β' -hydroxydipropylamine distilled at 110-116° (7-9 mm) as a yellow liquid.

Found %: N 9.59; OCH_3 20.72. $C_7H_{17}O_2N$. Calculated %: N 9.52; OCH_3 21.08.

2-Methoxy-9-hydroxy-4-oxa-5-methyl-7-azadecane was distilled at 160-168° (4-6 mm).

Found %: N 6.70; OCH_3 15.37. $C_{10}H_{23}O_3N$. Calculated %: N 6.83; OCH_3 15.12.

The residue remaining in the flask was dissolved in water and carbon dioxide gas was precipitated as barium carbonate by addition of barium hydroxide. The yield was quantitative.

SUMMARY

1. The reaction of propylene oxide with cyanamide was studied.
2. A method for separating the substances obtained on a chromatography column packed with silica gel was developed.
3. It was shown that all products are derivatives of 2-iminoxazolidine-1,3.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

TRANSESTERIFICATION OF DIALKYLPHOSPHINOUS ACID ESTERS WITH GLYCERINE DERIVATIVES

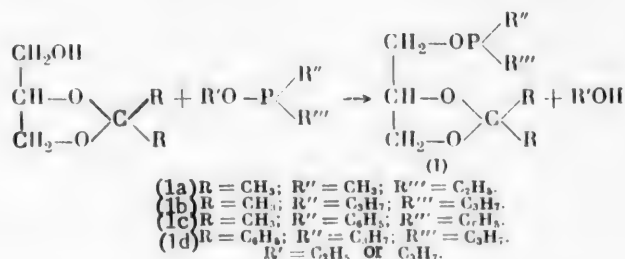
K. A. Petrov, É. E. Nifant'ev, and L. V. Khorkhoyanu

Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,
pp. 2889-2894, September, 1961

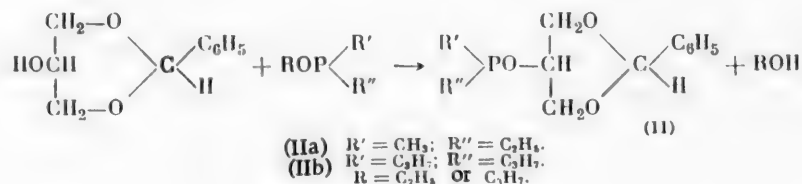
Original article submitted September 6, 1960

We previously demonstrated that dialkyl- and diarylphosphinous acid esters are easily transesterified by monohydric alcohols and ethylene glycol [1]. In this work we studied the transesterification of the indicated phosphinite derivatives with glycerine derivatives having one free hydroxyl group with the intent of expanding the scope and applications of the reaction. The synthesis of phosphinites and substituted glycerides has additional significance, for example, in connection with developing insect repellent preparations in the alkylideneglycerine [2, 3] and glycerine phosphate series [4].

The transesterification reaction was studied on sample glycerine derivatives containing a free primary or secondary hydroxyl. 1,2-Diphenylideneglycerine and 1,2-isopropylideneglycerine were used as derivatives of the first type. It was shown that these compounds undergo transesterification easily with simple esters of methylethyl-, dipropyl-, and diphenylphosphinous acids.

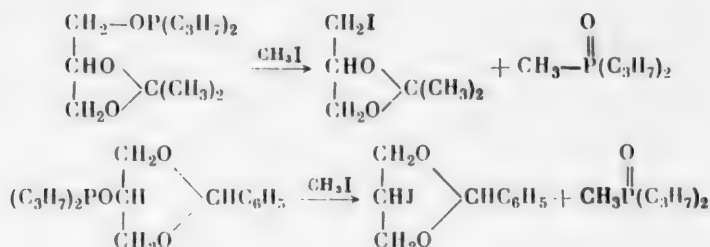


The transesterification of 1,3-benzylideneglycerine, which we selected as a derivative of glycerine containing a free secondary hydroxyl, with phosphinites occurs with more difficulty. However, even here good yields of the corresponding phosphinites are obtained.



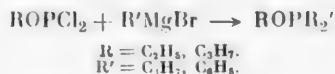
These glyceryl phosphinites, previously unreported compounds, are colorless liquids or crystalline substances with unpleasant odors which are easily oxidized in air but are unchanged during storage under an atmosphere of inert gas. In their chemical properties the products obtained resemble simple esters of dialkyl- and diarylphosphinous acids. Thus, by reaction with oxidizing agents or sulfur they are converted to the corresponding phosphonates and thiophosphonates. It should be mentioned that phosphinites formed from 1,2-isopropylideneglycerine are more easily converted to derivatives of pentavalent phosphorus, than phosphinites formed from 1,3-benzylideneglycerine, apparently owing to steric factors.

The phosphinites prepared took part in the Arbuzov reaction forming a phosphine oxide and the corresponding halo derivative. In the case given, the phosphinite formed from 1,2-isopropylidene glycerine reacted more energetically than the phosphinite formed from 1,3-benzylidene glycerine.



The transesterification and alkylation reactions of phosphinites can be utilized for obtaining some halo derivatives of polyhydric alcohols in cases when these halo derivatives are inaccessible or accessible with difficulty by other methods. We currently used this reaction for obtaining several complex halo derivatives of monohydric alcohols.

The propyl ester of dipropylphosphinous acid and the ethyl ester of diphenylphosphinous acid which were needed for this investigation were prepared by reacting Menshutkin's acid chloride with organomagnesium compounds at -70° .



The first of the esters prepared was a previously unknown compound; the second was previously synthesized by a more complex route.

EXPERIMENTAL

Transesterification of dialkylphosphinite esters with glycerol derivatives. A mixture of phosphinite and glycerine derivative, taken in equimolar amounts, and a little piece of sodium, was placed in a distillation apparatus. The reaction mixture was heated in a stream of dry and oxygen-free nitrogen until almost the calculated amount of ethyl (propyl) alcohol was distilled and the compound obtained was distilled under vacuum. The times, reaction temperatures yields, and constants of the compounds obtained are given in the table.

Oxidation of propyl dipropylphosphinite. In a flask cooled to -10° nitric oxide in a stream of dry nitrogen [5] was passed into propyl dipropylphosphinite. After the reaction mixture acquired a persistent green color, the reaction was finished and the excess oxidant was separated from the remaining reaction mixture under vacuum. After vacuum distillation pure propyl dipropylphosphinate was obtained in 70% yield.

B. p. $103-104^\circ$ (1 mm), n_D^{20} 1.4418, d_4^{20} 0.9543, M_{RD} 53.44; calc. 53.51.

Found %: P 16.04, 15.90. $\text{C}_9\text{H}_{21}\text{O}_2\text{P}$. Calculated %: P 16.14.

It is a colorless, odorless liquid which is insoluble in water but soluble in ether, benzene, carbon tetrachloride, and petroleum ether.

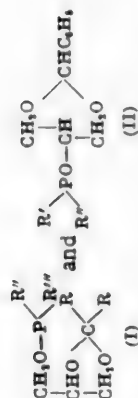
Oxidation of 1,2-isopropylidene [glyceryl] dipropylphosphinite (Ib). In a manner similar to that described above 2.4 g (53.5%) of 1,2-isopropylideneglyceryl dipropylphosphinate was obtained from 3.8 g of phosphinite.

B. p. $143-144^\circ$ (0.2 mm), n_D^{20} 1.4530, d_4^{20} 1.0376, M_{RD} 68.61; calc. 68.21.

Found %: P 11.45, 11.25. $\text{C}_{12}\text{H}_{25}\text{O}_4\text{P}$. Calculated %: P 11.74.

It is a colorless odorless liquid which is insoluble in water and petroleum ether but soluble in alcohol, acetone, chloroform, and dioxane.

Oxidation of 1,3-benzylideneglyceryl dipropylphosphinite (IIb). By the procedure described above 5.7 g (95%) of 1,3-benzylideneglyceryl dipropylphosphinate was prepared from 5.7 g of the phosphinite dissolved in 14 ml of anhydrous carbon tetrachloride.



No.	R	R'	R''	Time (in hr)	Temper-ature	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	M_R		Empirical formula	% P		(% up) pt. 1.1
									found	calc.		found	calc.	
(Ia)	CH ₃	—	—	3	120°	87.5—88.5° (7)	1.4485	1.0043	55.45	55.79	C ₉ H ₁₉ O ₃ P	15.01, 15.02	15.05	68
(Ib)	CH ₃	—	CH ₃	3	170—175	125—126° (7)	1.4518	0.9638	69.39	69.64	C ₁₂ H ₂₃ O ₃ P	12.40, 12.43	12.50	70
(Ic)	CH ₃	—	C ₃ H ₇	3	160—165	106.5—107° (10 ⁻⁴)	1.5687	1.1508	89.93	90.15	C ₁₈ H ₂₁ O ₃ P	9.81, 10.01	9.52	70
(Id)	C ₆ H ₅	—	C ₃ H ₇	4	175—180	104—105° (10 ⁻²)	—	—	—	—	C ₂₂ H ₂₉ O ₃ P	7.99, 8.29	8.33	50
(IIa)	—	CH ₃	—	4	145—150	T. n.t. 39—40	—	—	—	—	C ₁₃ H ₁₇ O ₃ P	12.64, 12.77	12.22	51
(IIb)	—	C ₃ H ₇	—	4	185—190	T. n.t. 49—50.5 T. n.t. 73—74	—	—	—	—	C ₁₆ H ₂₃ O ₃ P	10.74, 10.81	10.47	52

B. p. 117–118° (10⁻⁴ mm), n_D^{20} 1.5190.

Found %: C 61.13, 61.24; H 7.91, 7.83.
C₁₆H₂₅O₄P. Calculated %: C 61.54; H 8.01.

It is a very viscous liquid, tinted slightly yellow, which is insoluble in water and petroleum ether but soluble in alcohol, acetone, benzene, and carbon tetrachloride.

Addition of sulfur to propyl dipropylphosphinite. Sulfur* (0.48 g) was gradually added to 2.64 g of phosphinite. The reaction occurred with evolution of heat to 140–142°, at the conclusion of which the reaction mixture was heated 3 hr more at 110–115°. The reaction mixture was cooled, filtered, and distilled under vacuum. Propyl dipropylthiophosphinate was obtained (2.7 g; 90%).

B.p. 81–82° (0.5 mm), n_D^{20} 1.4778, d_4^{20} 0.9614, M_R 61.22; calc. 61.80.

Found %: P 14.36, 14.57; S 15.01, 15.10.
C₉H₂₁OSP. Calculated %: P 14.85; S 15.39.

It is a colorless liquid with an unpleasant odor which is insoluble in water and soluble in common organic solvents.

Addition of sulfur to 1,2-isopropylidene-glycerol dipropylphosphinite (Ib). By the method described above 3.9 g (93%) of 1,2-isopropylidene-glycerol dipropylthiophosphinate was obtained from 3.72 g of phosphinite and 0.48 g of sulfur.

B. p. 141–142° (1 mm), n_D^{20} 1.4847, d_4^{20} 1.0500, M_R 76.39; calc. 76.51.

Found %: P 10.66, 10.57; S 11.01, 11.10.
C₁₂H₂₅O₃SP. Calculated %: P 11.07; S 11.42.

The liquid is slightly yellow in color with an unpleasant odor and is insoluble in water but soluble in the common organic solvents.

Arbuz rearrangement of propyl dipropylphosphinite and methyl iodide. To 3.52 g of the phosphinite with cooling by ice bath was added 3 g of methyl iodide. At the conclusion of the exothermic reaction 3.6 g (~100%) of propyl iodide (b.p. 100–102.5°; n_D^{20} 1.5045) was distilled from the reaction mixture. After vacuum distillation of the residue 2.7 g (90%) of dipropylmethylphosphine oxide was obtained.

B.p. 91–93° (1 mm), m.p. 39–39.5°.

Found %: P 20.70, 20.70. C₇H₁₇OP. Calculated %: P 20.94.

* The sulfur used must be carefully dried.

It is colorless needles with an unpleasant odor which are slightly soluble in water and petroleum ether and very soluble in alcohol and acetone.

Reaction of 1,2-isopropylideneglyceryl dipropylphosphinite (Ib) with methyl iodide. In the manner described above 1.8 g (61%) of dipropylmethylphosphine oxide boiling at 131-132° and melting at 39-39.5° and 3 g (66.3%) of 2,2-dimethyl-4-iodomethyldioxolane-1,3 were obtained from 3.72 g of phosphinite and 2.13 g of methyl iodide.

M.p. 81-83° (9 mm), n_D^{20} 1.5038, d_4^{20} 1.6462.

Found %: C 29.81, 30.03; H 4.57, 4.46. $C_6H_{11}O_2I$. Calculated %: C 29.83; H 4.59.

Literature data [6]: b.p. 79° (10 mm), n_D^{20} 1.5046, d_4^{20} 1.6480.

After hydrolysis of 1,2-acetoneglyceryl iodide, α -glyceryl iodide melting at 47-48° was obtained. Literature [8]: m.p. 48.5-49.5°.

Reaction of 1,3-benzylideneglyceryl dipropylphosphinite (IIb) with methyl iodide. In the manner described above 0.6 g (50%) of dipropylmethylphosphine oxide boiling at 132-136° (9 mm) and melting at 38-39° and 0.6 g of 2-phenyl-5-iododioxane-1,3 boiling at 117-120° (9 mm), n_D^{20} 1.4983 (test for presence of iodine was positive) was obtained from 2.5 g of phosphinite and 1.42 g of methyl iodide. The substance [dioxane] decomposed upon further purification.

β -Iodoglycerine melting at 51.5-52° was obtained by hydrolysis of 1,3-benzylideneglyceryl iodide. Literature [8]: m.p. 53°.

Preparation of propyl dipropylphosphinite. To a mixture of 16.1 g of propyldichlorophosphite and 34.8 g of pyridine in 150 ml of absolute ether at -70° was gradually added a solution of 0.22 g-mole of propyl magnesium bromide in 150 ml of absolute ether. The rate of adding the organomagnesium compound must be such that the temperature in the reaction flask does not exceed -65°. After the reagents were mixed, the reaction mixture was gradually warmed to room temperature; the residue was removed by filtration, the ether was evaporated, and the remaining oil was distilled under vacuum. All operations must be conducted in an atmosphere of purified nitrogen. After two distillations propyl dipropylphosphinite (6 g; 46.6%) was obtained.

B. p. 70-71° (7 mm), n_D^{20} 1.4430, d_4^{20} 0.8473, M_R 54.64; calc. 54.94.

Found %: P 17.18, 16.93. $C_9H_{21}OP$. Calculated %: P 17.62.

It is a colorless mobile liquid with an unpleasant odor which is insoluble in water, but is easily miscible with common organic solvents. The substance ignites in air.

Preparation of ethyl diphenylphosphinite. In the manner described above 9 g (64%) of ethyl diphenylphosphinite boiling at 127-128° (1 mm), n_D^{20} 1.5910, was prepared from 9 g of ethyldichlorophosphite, 15 g of pyridine in 120 ml of absolute ether and 0.124 g-mole of phenyl magnesium bromide in 70 ml of absolute ether. Salt with cuprous iodide, m.p. 190-192°. Literature [7]: b.p. 179° (17 mm), salt with cuprous iodide, m.p. 190-191°.

SUMMARY

1. The transesterification reaction between dialkylphosphinite esters and glycerine derivatives having free primary or secondary hydroxyls was studied. A previously unknown series of glyceryl phosphinites was obtained.
2. Some chemical properties of the phosphinites obtained were studied.
3. Propyl dipropylphosphinite and ethyl diphenylphosphinite were synthesized by the reaction of Menshutkin's acid chlorides with organomagnesium compounds.

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CONJUGATION FACTORS IN CYCLIC SYSTEMS

III. SOME SPECTRAL RULES FOR A SERIES OF ISOMERIC CYCLO- HEXADIENE-1,2-DICARBOXYLIC ACIDS AND THEIR DERIVATIVES

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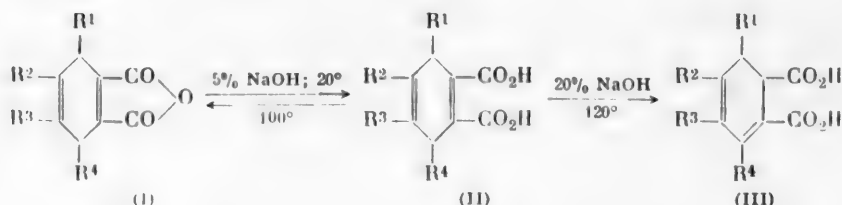
N. D. Zelinskii Institute for Organic Chemistry

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pp. 2894-2898, September, 1961

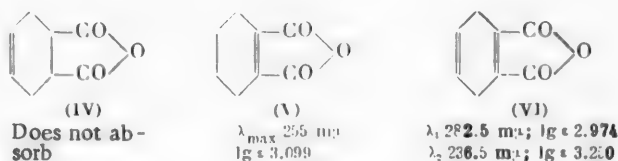
Original article submitted September 18, 1960

In the process of defining a rule for the isomerization of endocyclic double bonds we synthesized methyl- and dimethylcyclohexadiene-1,2-dicarboxylic acids of the type (II) and (III) and their functional derivatives for which we investigated some interconversions [1, 2].



The subject of this communication is the examination of UV- and IR-absorption spectra of these compounds.

As was shown previously [3] the characteristic UV-absorption spectrum of anhydride type (I) contains two maxima (λ_1 235-245 m μ and λ_2 280-290 m μ) while the corresponding acids and their dimethyl esters exhibit only one discontinuity in the UV-absorption curve in the 235-245 m μ region. Comparison of these data allows the conclusion that the long-wave absorption peak in the UV-spectrum of anhydrides (I) is present in compounds classified as having a Δ^1 -double bond and the CO-bond of the anhydride ring in their structure. The absence of this peak in the spectra of acids (II) and their esters is connected, apparently, to steric interference with coplanarity of the Δ^1 -double bond and the CO-bond of the carbonyl group [1] in these compounds.



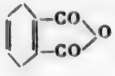
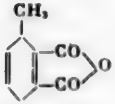
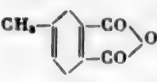
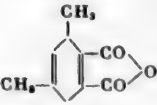
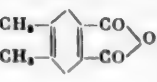
Comparison of the UV-absorption spectra of anhydrides (IV)-(VI) in turn shows that introduction of a second formally isolated double bond into the Δ^4 -position of anhydride (V) leads not only to displacement of the absorption peak characteristic for anhydride (V) into the longer-wave region but also to appearance of a new peak of appreciable intensity. As a result of the systematic study of UV-absorption spectra of all the previously-prepared compounds [1, 2] we established that they all contain an absorption peak in the region 235-245 m μ (Table 1).

The anomalous UV-spectra of the anhydrides considered is caused, apparently, by the presence of non-classical electronic interactions between the formally isolated C = C bonds in their molecules. This interaction also occurs, if only to a small extent, in the molecules of corresponding acids and esters is shown in their UV-spectra by a discontinuity in the 235-245 m μ region of the absorption curve. The possible existence of such a side-effect of conjugation was previously noted in the literature and was used to explain the anomaly found in the UV-absorption

TABLE 1. UV-Absorption Spectra of Isomeric Cyclohexadiene-1,2-Dicarboxylic Acids and Their Anhydrides

Acid (in ethanol)	λ_{\max} (m μ)	lg ϵ	Anhydride (in acetonitrile)	λ_{\max} (m μ)	lg ϵ	Anhydride (in acetonitrile)	λ_{\max} (m μ)	lg ϵ
	—	—		298.5	3.719		236.5	3.250
	288	3.671		302	3.836		240.5	3.443
	296	3.903		313.5	4.027		244.5	3.388
	298 297.5	3.793 3.904		315	3.948		246	3.443
	293.5 293	3.899 3.875		314 312.5	3.938 3.778		248	3.446
	285 286	3.793 3.846		303.5 303.5	3.965 3.773		243	3.342
	303	3.953		325	3.890		249.5	3.389
								2.556

TABLE 2. Characteristic Absorption for Methyl- and Dimethyl- $\Delta^{1,4}$ -Cyclohexadiene-1,2-dicarboxylic Anhydrides in the 1700-1600 cm^{-1} Region

$\Delta^{1,4}$ -Anhydride	ν_1 cm^{-1}	ν_2 cm^{-1}
	1640	1687
	1643	1687
	1650	1690
	1645	1687
	1647	1690

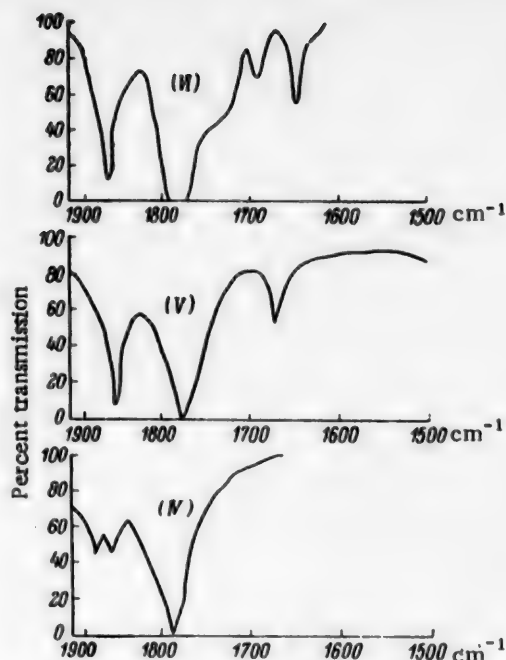


Fig. 1. IR-spectra for anhydrides of Δ^1 -(V) and Δ^4 -cyclohexen-(IV) and $\Delta^{1,4}$ -cyclohexadiene-1,2-dicarboxylic acids (VI) (taken on IKS-12 spectrograph with NaCl prism, 1% solution in chloroform).

spectra of ketones in the cyclodecene series [4-6], as well as for ketones and esters of the $\Delta^{1,4}$ -cyclohexadiene monocarboxylic acid and bicycloheptadiene series [7-9]. The recently recorded ability of bicyclo(2,2,0)heptadiene-2,5 to enter into the diene synthesis in the role of "diene component" [10, 11] serves as definite chemical confirmation for the presence of such an effect.

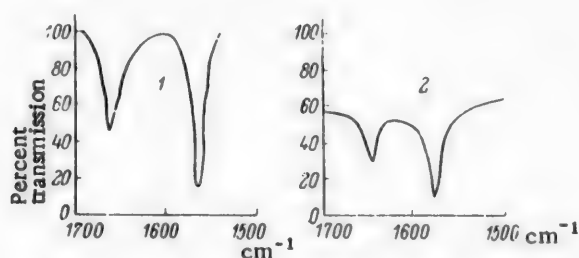


Fig. 2. IR-spectra for the anhydride (1) and diester of $\Delta^{4,6}$ -cyclohexadiene-1,2-dicarboxylic acid (2).

The UV-spectra of isomeric $\Delta^{4,6}$ -dicarboxylic acids (III) and their anhydrides exhibit only one normal absorption band, corresponding to a system of conjugated double bonds (Table 1). As is seen from the data in Table 1, the differences recorded in the absorption spectra for $\Delta^{1,4}$ - and $\Delta^{4,6}$ -anhydrides is somewhat specific, and can be used as a method for structural proof.

With the intention of further studying the effects of double bond conjugation in the $\Delta^{1,4}$ -cyclohexadiene-1,2-dicarboxylic acid series we took the IR-absorption spectra of type (I) anhydrides in the 1900-1500 cm^{-1} region, where $\text{C}=\text{C}$ and $\text{C}=\text{O}$ valence vibrations are generally found. Comparison of the IR-absorption spectra of Δ^1 - and Δ^4 -cyclohexene-1,2-dicarboxylic anhydrides with spectra of $\Delta^{1,4}$ -cyclohexadiene-1,2-dicarboxylic anhydrides allowed

discovery of a characteristic five-membered anhydride ring absorption band at $1788\text{--}1770\text{ cm}^{-1}$ and $1855\text{--}1850\text{ cm}^{-1}$ [12] in all of these anhydrides. The existence of spectral differences among these anhydrides was observed in the $1700\text{--}1600\text{ cm}^{-1}$ region, where carbon-carbon double bond valence vibrations generally show a band (Fig. 1).

As is seen from Fig. 1, the Δ^4 -anhydride does not exhibit absorption of marked intensity in this region, while the Δ^1 -anhydride under comparable conditions has an absorption maximum at 1668 cm^{-1} , i.e., in the region characteristic for carbon-carbon double bonds conjugated with a carbonyl group [12]. In contrast to this, $\Delta^{1,4}$ -cyclohexadiene-1,2-dicarboxylic anhydride has two absorption bands in this region ($\nu_{1\text{max}} 1687\text{ cm}^{-1}$; $\nu_{2\text{max}} 1640\text{ cm}^{-1}$); the corresponding diester has the same absorption character.

The presence of two absorption bands in the $1700\text{--}1600\text{ cm}^{-1}$ region is characteristic of all previously-described [1, 2] methyl- and dimethyl- $\Delta^{1,4}$ -cyclohexadiene-1,2-dicarboxylic anhydrides (Table 2) and can serve along with the UV-absorption spectra considered above as a convenient criterion for identifying derivatives of cyclohexadienecarboxylic acid with $\Delta^{1,4}$ -double bond systems.

In contrast to the system with $\Delta^{1,4}$ -position of double bonds the anhydride and diester of $\Delta^{4,6}$ -cyclohexadiene-1,2-dicarboxylic acid have only one absorption band in the $1700\text{--}1600\text{ cm}^{-1}$ region. Besides this they exhibit intense absorption in the 1580 cm^{-1} region. Characteristics of their spectra are given in Fig. 2.

The IR-absorption spectra presented above for compounds with $\Delta^{4,6}$ -placement of endocyclic double bonds are additional criteria for identifying isomeric cyclohexadiene-1,2-dicarboxylic acids and their derivatives.

SUMMARY

Characteristic rules for IR- and UV-spectra of methyl- and dimethyl- $\Delta^{1,4}$ - and $\Delta^{4,6}$ -cyclohexadiene-1,2-dicarboxylic anhydrides and dimethyl esters which can be used for spectral identification of cyclohexadiene systems with $\Delta^{1,4}$ - and $\Delta^{4,6}$ -position of the double bonds were established.

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INVESTIGATION IN THE FURAN SERIES

XVII. SYNTHESIS OF AMINO ALCOHOLS OF THE 3,6-

ENDOXYCYCLOHEXANE SERIES

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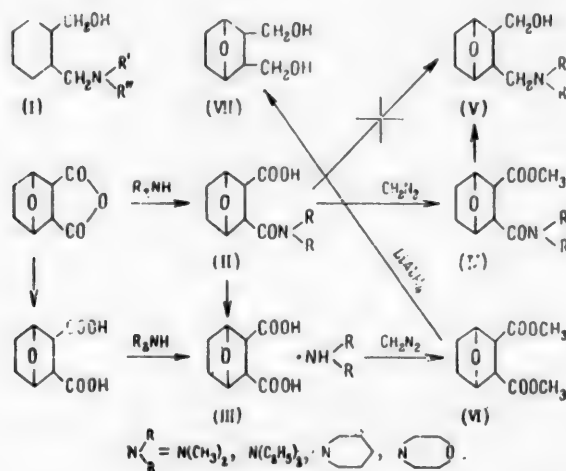
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

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Original article submitted October 5, 1961

Amino alcohols of the aliphatic, aromatic, alicyclic and heterocyclic series are physiologically active and some of them have been used as hypotensive agents. Rice and his co-workers [1] showed that amino alcohols of the cyclohexane series (I) have a marked hypotensive effect. Investigating the effect of structure on the hypotensive activity of various N-substituted derivatives of perhydroisoindole, they established that the presence of 1,4-endoxy bridge in the cyclohexane ring reduces markedly the toxicity and increases the hypotensive activity [2]. The methiodide of N-dimethylamino-4-methyl-4,7-endoxyperhydroisoindole has been recommended for practical use [3].

In this work we synthesized amino alcohols of the endoxocyclohexane series, with the general formula (V): the reaction of the anhydride of exo-3,6-endoxyhexahydrophthalic acid with secondary amines led to the corresponding monoamides of this acid (II), which, however, could not be obtained in the analytically pure state because they hydrolyze extremely readily to the corresponding monoammonium salts (III). When dissolved in water and evaporated on a watch glass the monoamides (II) pass over to the corresponding monoammonium salts (III). Therefore, even if only traces of moisture are present in the reaction mixture the monoamides are obtained as a mixture with the corresponding monoammonium salts, which complicates markedly the synthesis of monoamides; for comparison, we obtained these salts separately.



Mel'nikov and Kraft [4] described N,N-diethyl-oxa-cis-3,6-endoxyhexahydrophthalamic acid (IIb) and noted that it does not have a herbicidal activity. However, a comparison of the melting points of the compounds we obtained with the melting point indicated in [4] leads to the conclusion that in actual fact these authors were dealing with the corresponding ammonium salt (IIb) or a preparation containing a preponderant amount of the latter.

Reduction of the monoamides (II) by lithium aluminum hydride to the corresponding amino alcohol (V) could not be achieved in ether or in tetrahydrofuran or dibutyl ether. Therefore we reduced the monomethyl esters of

monoamido-oxa-3,6-endoxyhexahydrophthalic acid (IV), which were obtained by methylating the monoamides (II) with diazomethane. Methylation of the corresponding ammonium salts (III) led to the cis-dimethyl ester of 3,6-endoxyhexahydrophthalic acid (VI), admixture of which with the monomethyl ester of monoamide (IV) would be undesirable because the products of its reduction are difficult to separate from the corresponding amino alcohol. An admixture of the dimethyl ester (VI) is most conveniently determined by a physiological sample because it has a marked blister-producing effect on skin, with an incubation period of about 10-12 hours [5]. It is of interest that neither 4-hydroxy [6] nor 4,5-epoxy [7] substituted analogs of cis-dimethyl ester have a blister-producing effect, whereas the trans-dimethyl ester of 3,6-endoxyhexahydrophthalic acid has such an effect.

When reduced by lithium aluminum hydride in ether, monoestermonoamides (IV) readily give the corresponding amino alcohols of the 3,6-endoxycyclohexane series (V), substituted at the nitrogen atom; these are obtained in the form of colorless viscous liquids with yields from 63 to 87%. The methiodides of these amino alcohols, obtained by boiling with excess methyl iodide, are white hygroscopic substances.

Since in the presence of admixture of the dimethyl ester of 3,6-endoxyhexahydrophthalic acid (VI) the amino alcohols (V) obtained were contaminated by its reduction products, we investigated the reduction of (VI) separately under different conditions.

In [8] it is indicated that when the dimethyl ester of 3,6-endoxyhexahydrophthalic acid (VI) is reduced by lithium aluminum hydride in ether, only one carbomethoxyl group is reduced, and complete reduction is only obtained in tetrahydrofuran. However, we found that in an ether solution under the conditions of the reduction of monoester-monoamides (IV) the reaction takes place with the formation of the corresponding diol, 1,2-dimethylol-3,6-endoxycyclohexane (VII), and that the course of the reduction of the dimethyl ester of 3,6-endoxyhexahydrophthalic acid (VI) is independent of the choice of solvent if an excess of lithium aluminum hydride is used and reduction is carried out for a long time.

EXPERIMENTAL

Oxa-cis-3,6-endoxyhexahydrophthalic acids. 0.1 g-mole of the anhydride of 3,6-endoxyhexahydrophthalic acid was dissolved in 100 ml of anhydrous benzene in a flask with a reflux condenser and 0.11 g-mole of secondary amine, distilled over sodium, was added; the mixture was boiled for half an hour and was allowed to stand at room temperature for 10 days. Monoamides (IIb-d), precipitated in crystalline form, were filtered. Monoamide (IIa) was obtained as an oil when the solvent was distilled. The yield was quantitative.

Monoammonium salts of oxa-cis-3,6-endoxyhexahydrophthalic acid (IIIa-d). 1 g of the anhydride of 3,6-endoxyhexahydrophthalic acid was dissolved in a mixture of 10 ml of dioxane and 5 ml of water in a flask with a reflux condenser; the mixture was boiled for 1 hour, an equimolecular amount of secondary amine was added and it was left overnight. The melting points and analytical data of the compounds obtained are given in Table 1.

Methyl esters of oxa-cis-3,6-endoxyhexahydrophthalic acids (IVa-d). 0.1 g-mole of the corresponding monoamino acid (II) was added in small amounts with constant stirring to an ether solution of diazomethane (70% excess). When liberation of nitrogen had ceased the ether was evaporated and the residue was crystallized from petroleum ether. The yield was quantitative. The constants of the compounds obtained are given in Table 2.

The dimethyl ester of oxa-cis-3,6-endoxyhexahydrophthalic acid was obtained by methylating the monoammonium salts (III) by the above-indicated method. The m.p. was 75° (from petroleum ether).

Found %: C 56.20, 56.27; H 6.77, 6.96. $C_{10}H_{14}O_5$. Calculated %: C 56.07; H 6.59.

Literature data: m.p. 80-85° [5], 76° [9].

Reduction of the methyl esters of oxa-cis-3,6-endoxy-N,N-dialkylhexahydrophthalic acids. 0.1 g-mole of finely ground (IVa-d) in powdered form was added in portions to a stirred 1 N ester solution of lithium aluminum hydride (150% excess); it was boiled for 50 hours, decomposed with the calculated amount of water and the mixture was extracted with boiling chloroform; the solvent was driven off and the residue was distilled under vacuum.

Oxa-cis-1-methylol-2-dimethylaminomethyl-3,6-endoxycyclohexane. 12.5 g (68%) was obtained in the form of a viscous oil.

B.p. 82° (0.3 mm), n_D^{20} 1.4873.

Found %: C 64.75, 64.93; H 10.30, 10.35. $C_{10}H_{19}O_2N$. Calculated %: C 64.82; H 10.33.

TABLE 1. N,N-Dialkyl Monoammonium Salts of 3,6-Endoxyhexahydrophthalic Acid (III)

Name of the N,N-dialkyl amino group and formula of the salt	Melting point	% C		% H	
		found	calculated	found	calculated
Dimethylamino $C_{10}H_{17}O_5N$	152–153°	52.17, 52.19	51.93	7.57, 7.52	7.41
Diethylamino $C_{12}H_{21}O_5N$	136–137	55.65, 55.59	55.58	8.02, 8.19	8.16
Piperidino $C_{13}H_{21}O_5N$	146	57.60, 57.60	57.54	7.89, 7.83	7.80
Morpholino $C_{12}H_{19}O_5N$	157	52.58, 52.43	52.73	6.98, 6.92	7.00

TABLE 2. Methyl Esters of 3,6-Endoxy-N,N-Dialkylhexahydrophthalic Acids (IV)*

Name of N,N-dialkyl amino group and formula of the ester	Melting point	% C		% H	
		found	calculated	found	calculated
Diethylamino- $C_{13}H_{21}O_4N$	81°	61.51, 61.29	61.16	8.53, 8.50	8.29
Piperidino- $C_{14}H_{21}O_4N$	103	62.69, 62.74	62.93	8.09, 7.90	7.91
Morpholino- $C_{13}H_{19}O_4N$	136	58.11, 58.18	57.97	7.13, 7.20	7.11

* The diethylamino ester was obtained as an oil and was used in the reaction without additional purification.

Methiodide, m.p. 164–165°.

Found %: C 40.60, 40.29; H 6.97, 7.12. $C_{11}H_{22}O_2NI$. Calculated %: C 40.37; H 6.77.

Oxa-cis-1-methylol-2-diethylaminomethyl-3,6-endoxycyclohexane. 17.0 g (80%) was obtained in the form of a viscous oil.

B.p. 92° (0.3 mm), n_D^{20} 1.4858, d_4^{20} 1.0242, MR_D 59.77; calc. 60.32.

Found %: C 67.67, 67.46; H 10.92, 10.92. $C_{22}H_{28}O_2N$. Calculated %: C 67.56; H 10.87.

Methiodide, m.p. 132–132.5° (washed with acetone).

Found %: C 43.76, 44.03; H 7.23, 7.22. $C_{25}H_{26}O_2NI$. Calculated %: C 43.95; H 7.38.

Oxa-cis-1-methylol-2-piperidinomethyl-3,6-endoxycyclohexane. We obtained 19.6 g (87%) in the form of a viscous oil.

B.p. 120–123° (0.3 mm), n_D^{20} 1.5049.

Found %: C 69.74, 69.56; H 10.34, 10.55. $C_{25}H_{28}O_2N$. Calculated %: C 69.29; H 10.28.

Methiodide, m.p. 121–122° (washed with acetone).

Found %: C 45.81, 45.97; H 7.40, 7.50. $C_{14}H_{26}O_2NI$. Calculated %: C 45.78; H 7.13.

Oxa-cis-1-methylol-2-morpholinomethyl-3,6-endoxycyclohexane. 14.3 g (63%) was obtained in the form of a very viscous oil.

B.p. 133° (0.3 mm), n_D^{20} 1.5080.

Found %: C 63.54, 63.67; H 9.40, 9.39. $C_{22}H_{21}O_3N$. Calculated %: C 63.49; H 9.31.

Methiodide, m.p. 205° (with decomp.).

Found %: C 42.12, 42.29; H 6.44, 6.59. $C_{12}H_{24}O_3NI$. Calculated %: C 42.28; H 6.56.

Oxa-cis-1,2-dimethylol-3,6-endoxycyclohexane. 11 g (70%) with a m.p. of 62°* was obtained by the above-indicated method.

Bis-phenylurethan. 1.4 g of diol and 1.8 ml of phenyl isocyanate was boiled for 10 minutes on an oil bath; the m.p. was 170-171° (from benzene).

Found %: C 66.89, 66.78; H 6.30, 6.28. $C_{22}H_{24}O_5N_2$. Calculated %: C 66.65; H 6.10.

SUMMARY

Reduction of the methyl esters of oxa-cis-3,6-endoxyhexahydrophthalamic acids by lithium aluminum hydride may serve as a convenient method of synthesizing oxa-cis-1-methylol-2-N,N-dialkylaminomethyl-3,6-endoxycyclohexanes.

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* Literature data: m.p. 104° [8], m.p. 62.5° [9].

REACTIONS OF AROMATIC NITRO COMPOUNDS

XI. INVESTIGATION OF THE RE-ESTERIFICATION REACTION

BY THE ISOTOPIC METHOD

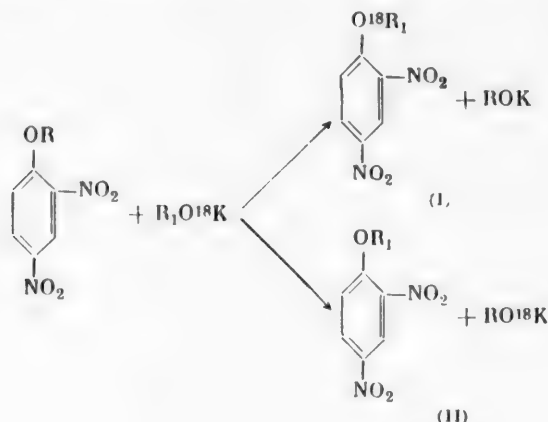
S. S. Gitis, M. O. Tereshkevich, L. I. Garus,

A. I. Glaz, and O. K. Skarre

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An investigation of the re-esterification of alkyl esters of 2,4-dinitrophenyl by means of labeled atoms makes it possible to determine how alkyl radicals in dinitro esters are replaced. The re-esterification process may be represented in general form as follows:



To prove which one of these paths the process takes, we investigated the re-esterification of dinitroanisole to dinitrophenetole by means of ethyl alcohol containing a heavy oxygen isotope. The results of the investigations showed that 2,4-dinitrophenetole containing the heavy oxygen isotope O^{18} is always formed in this reaction. Therefore the re-esterification reaction takes place according to system (I), which again confirms the mechanism of the reaction, including the formation of an intermediate product of the quinol type [1, 2].

The data of the investigations makes it possible to conclude that the re-esterification reaction may serve as an easy and convenient method of obtaining dinitro esters with a labeled oxygen atom.

It was previously established [3, 4] that small amounts (10-15%) of 2,4-dinitrophenol are formed together with esters of 2,4-dinitrophenol during the process of the re-esterification reaction. Naturally, the investigation of the hydrolysis reaction of alkyl esters of 2,4-dinitrophenol was of great interest. For this purpose, 2,4-dinitrophenol containing a heavy oxygen isotope was subjected to alkaline hydrolysis.

Hydrolysis of the ester may be accompanied either by removal of $\text{O}^{18}\text{C}_2\text{H}_5$ or C_2H_5 . The investigations established that the liberated alcohol contains all the O^{18} isotope; therefore the $\text{O}^{18}\text{C}_2\text{H}_5$ group is removed during the process of hydrolysis, i.e., hydrolysis takes place at the point of rupture of the $\text{Ar}-\text{O}$ bond.

It is interesting to note that when the alcohol containing a heavy oxygen isotope is burnt, the latter is converted entirely to water. For this reason it may be assumed that the first stage of the oxidation of the alcohol is the formation of a molecule of water by the hydroxyl group and the hydrogen atom combined with the carbon atom of

the chain. Any other oxidation mechanism must lead to redistribution of the oxygen of the alcohol between water and carbon dioxide. The content of the heavy oxygen isotope in the ethyl alcohol may be determined by its reduction or oxidation, followed by analysis of the water obtained. The somewhat lower content of O^{18} in the water after combustion of the alcohol compared with the figure obtained when the latter is reduced may probably be explained by the presence of a slight oxygen exchange between the water vapor and CuO . However, the loss caused by this is slight and in quite a number of cases it may be neglected.

EXPERIMENTAL

Synthesis of dinitrophenetole labeled with O^{18} . 22.4 g of caustic potash in 50 ml of alcohol containing the heavy oxygen isotope was added in portions (while cooling) to a solution of 40 g of dinitroanisole in 200 ml of dioxane [5]. In 30 minutes after commencement of the addition of the alcoholic solution of caustic potash the dark-red complex was broken up with a small amount of water. 34 g (83%) of dinitrophenetole was obtained.

Saponification of 2,4-dinitrophenetole labeled with O^{18} . 32.5 g of 2,4-dinitrophenetole was added to a solution of 10 g of caustic potash in 150 ml of water and the contents were boiled for 14 hours. After acidification of the reaction mixture the alcohol was distilled twice with a herringbone fractionating column. 9.5 g of alcohol containing 3.44 % water, was obtained.

Analysis of ethyl alcohol for the O^{18} content. A. Reduction of ethyl alcohol. 10 ml of alcohol was reduced by hydrogen to hydrocarbons and water on a nickel catalyst at 450-550°. Hydrogen sulfide was first removed from the hydrogen by passing it through a solution of lead acetate; the hydrogen was then dried with sulfuric acid and calcined $CaCl_2$.

The nickel catalyst was placed in a quartz tube from which the air had been displaced by hydrogen passing over it for 3 hours. The vessel was then connected to the alcohol, through which hydrogen was bubbled. The water vapor formed was condensed in a condenser connected to the tube. After careful purification the water was analyzed by a densimetric method [6]. The excess density of the alcohol was 248 γ , that of the initial alcohol was 250 γ .

B. Oxidation of ethyl alcohol labeled with O^{18} . 10 ml of heavy alcohol used in the reaction was passed together with air over cupric oxide at 700-800°. The alcohol was oxidized to carbon dioxide and water. The water was frozen in special traps, and the carbon dioxide was absorbed by a concentrated solution of caustic potash. After careful purification the water was investigated by the densimetric method. The excess density was 76 γ , and the dilution was $76 \gamma \cdot 3 = 228 \gamma$.* The solution of caustic potash which had absorbed the carbon dioxide was boiled for a long period, after which the water was distilled from it. Analysis of this water by the densimetric method showed the absence of an excess amount of heavy oxygen isotope.

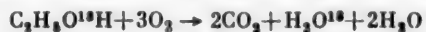
SUMMARY

1. By means of labeled atoms it was shown that the process of re-esterification of alkyl esters of 2,4-dinitrophenetole takes place with rupture of the Ar-O bond.
2. It was established that the OC_2H_5 group is removed during the hydrolysis of 2,4-dinitrophenetole.
3. 2,4-Dinitrophenetole labeled with heavy oxygen was synthesized.
4. It was shown that the alcohol may be analyzed for the heavy oxygen content by subjecting it to reduction or oxidation.

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* The concentration of heavy oxygen isotope in it was three-fold less than in the water obtained after reduction of the alcohol because as a result of the oxidation reaction, the water is diluted three-fold.



INVESTIGATIONS IN THE FIELD OF DIACYL PEROXIDE

I. SYNTHESIS AND PROPERTIES OF UNSYMMETRICAL DIACYL

PEROXIDE

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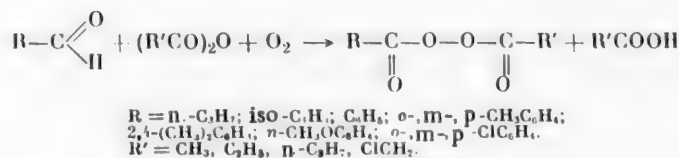
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As is known, unsymmetrical diacyl peroxide are obtained by reacting peracids with the acyl chlorides of acids [1, 2]. For unsymmetrical acetylbenzoyl peroxide there is another method of preparation, consisting in oxidation of a mixture of benzaldehyde and acetic anhydride by air [3-5]. In view of the fact that acetylbenzoyl peroxide is of interest as a polymerization initiator, the oxidation of benzaldehyde in acetic anhydride was investigated in detail [6], high yields of peroxide being obtained. Although the oxidation of aldehydes in the presence of acetic anhydride has been studied by many investigators [7] we are the first to have proposed the use of the oxidation of aldehydes in the presence of acid anhydrides as a general method, suitable for the synthesis of unsymmetrical diacyl peroxides. In a previous report [8], we described four unsymmetrical diacyl peroxides obtained by this method.

In the present work it was shown that unsymmetrical diacyl peroxides are obtained with high yields by oxidation with air (oxygen) of homologs and substituted benzaldehydes. In a similar way, when aliphatic aldehydes (n-butyric and isovaleric) in acetic anhydride are oxidized they give acetyl-n-butyryl and acetylisovaleryl peroxides, also with high yields.



Oxidation was carried out in two ways: by air in a circulating system, and by oxygen in a closed system. In the circulating system, apparatus similar to that used in [6] was employed. The temperature of the experiment varied from 20-25° in the case of aliphatic aldehydes, to 40-50° for aromatic aldehydes. The reaction was carried out in diffuse light or with irradiation by an electric lamp (50-75 W). The yield of peroxide did not increase with an increase in the amount of anhydride. Anhydrous sodium acetate or calcium carbonate was used as a catalyst for the reaction. The yields of peroxides obtained with sodium acetate were generally somewhat higher than with calcium carbonate; furthermore, considerably less sodium acetate is required. During synthesis with propionic anhydride, replacement of sodium acetate by sodium propionate did not improve the yield of peroxide. Diacyl peroxide was checked to see whether it contained acyl hydroperoxide [9], which was generally absent.

When air was passed at high rates, appreciable evaporation of the anhydride (in the presence of non-volatile aldehyde) was observed; therefore some of the experiments were carried out in a closed system with oxidation by oxygen and simultaneous stirring. The use of a closed system was particularly favorable in the case of volatile aldehydes as well. In this case, oxidation may also be checked by recording the amount of absorbed oxygen. For the rest, oxidation by oxygen does not have advantages compared with oxidation by air in a circulating system.

The peroxides obtained were liquid or solid substances with a characteristic rather pungent "peroxide" odor. Peroxides of the aliphatic series (acetyl-n-butyryl, acetylisovaleryl) and of the aromatic series (acetyl-o-methylbenzoyl, acetyl-2,4-dimethylbenzoyl, acetyl-o-chlorobenzoyl, propionylbenzoyl, propionyl-m-chlorobenzoyl, n-

butyrylbenzoyl and monochloroacetylbenzoyl) were liquid. The other peroxides were solid substances with a low melting point. The solid peroxides were readily isolated and were obtained with a high degree of purity after 1-2 recrystallizations. Liquid peroxides of the aromatic series were generally subjected to additional purification by treatment with nitric acid; however, in this case, too, they remained less pure than the solid peroxides.

Peroxides of the aliphatic series explode violently when introduced into the flame of a burner. However, spontaneous explosions were not observed during distillation or when the substance was kept for long periods. Aromatic peroxides have a less explosive character.

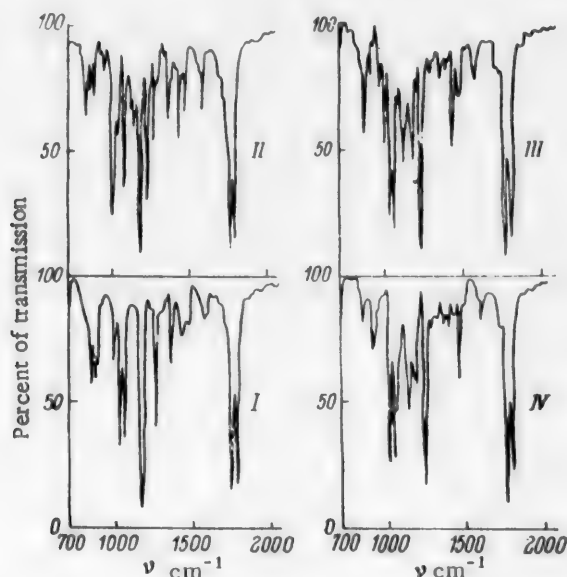


Fig. 1. Infrared transmission spectra of organic peroxides: 1) Acetyl-m-methylbenzoyl; II) acetyl-o-chlorobenzoyl; III) propionyl-m-chlorobenzoyl; IV) n-butyrylbenzoyl.

Aliphatic peroxides are stable on keeping. Thus, when acetyl-n-butyryl peroxide was kept for 4 months at a temperature of 1-2°, it lost only 7% of its activity, and under the same temperature conditions acetylisovaleryl peroxide retained its initial activity when kept for 2 months. Solid aromatic peroxides are stable when kept for long periods, even at room temperature. Acetyl-p-methoxybenzoyl peroxide decomposes somewhat when kept for long periods at room temperature. Liquid aromatic peroxides are less stable and decompose when kept for long periods at room temperature, the least stable being those containing C_2H_5COO- , $n-C_3H_7COO-$ and particularly $ClCH_2COO-$ groups. When propionyl-benzoyl and monochloroacetyl-benzoyl peroxides were kept for long periods or treated with soda, a symmetrical product was observed, the formation of a symmetrical peroxide – benzoyl peroxide – being proven in both cases.

When benzaldehyde was oxidized in the presence of benzoic anhydride, peroxide formation was slight.

When an attempt was made to oxidize m-nitrobenzaldehyde, p-nitrobenzaldehyde and p-dimethylamino-benzaldehyde in the presence of acetic anhydride, formation of peroxides was not observed.

For peroxides 2, 6, 11, 12, 13 and 14 (see table), infrared spectra in the region of transmission of an NaCl prism were obtained with an IKS-14 infrared spectrophotometer. 0.1 M solutions of peroxides in CCl_4 , using a thickness of the absorbent layer of 0.25 mm, were investigated (Figs. 1 and 2).

An interpretation of the infrared spectra of peroxides 3, 5, 7 and 8 was given in [8], and of peroxides 1, 4 and 9 in [10]. The infrared spectra of the aromatic peroxides differ from the spectra of the aliphatic peroxides although they have much in common and have a whole series of characteristic bands. A weak band at 845-860 cm^{-1} is observed in the spectra of all the peroxides, whereas the intense band in the 1000-1030 cm^{-1} region is contained only in the spectra of peroxides 2, 6, 10, 11 and 12 (Fig. 1, curves I, II, III and IV; Fig. 2, curve 1). The authors of [11, 12]

consider that the above-mentioned bands are characteristic of vibrations of the O—O group of aliphatic and aromatic peroxide compounds. An intense band at $1020\text{--}1050\text{ cm}^{-1}$ is also observed in the spectra of the latter. The intensity and position of its maximum depend on the character and position of the substituent in the ring. The presence of this band is evidently due to non-planar vibrations of the benzene ring. In the spectra of peroxides 14 and 13 (Fig. 2, curves II, III and IV) in this region of the spectrum ($1050\text{--}1060\text{ cm}^{-1}$) there is only one intense absorption band. A very intense band with a maximum at $1170\text{--}1175\text{ cm}^{-1}$ is observed in the spectra of peroxides 2, 6, 14 and 13 (Fig. 1, curves I and II, Fig. 2, curves II, III and IV). In this region, absorption is absent in the spectra of peroxides 10, 11 (Fig. 1, curves III and IV) and 12 (Fig. 2, curve I).

It may therefore be concluded that the above-mentioned frequency must be attributed to vibrations of the C—CH₃ group at the end of the chain. For aromatic peroxides the introduction of a CH₂ or CH₂Cl group alters the frequency of the vibrations, and in this region of the spectrum three weak bands, similar to the bands of the spectrum of compounds of the paraffin series, are observed. For peroxides 14 and 13 (Fig. 2, curves II, III and IV), in this region of the spectrum there is also an intense band with a maximum at $1145\text{--}1160\text{ cm}^{-1}$.

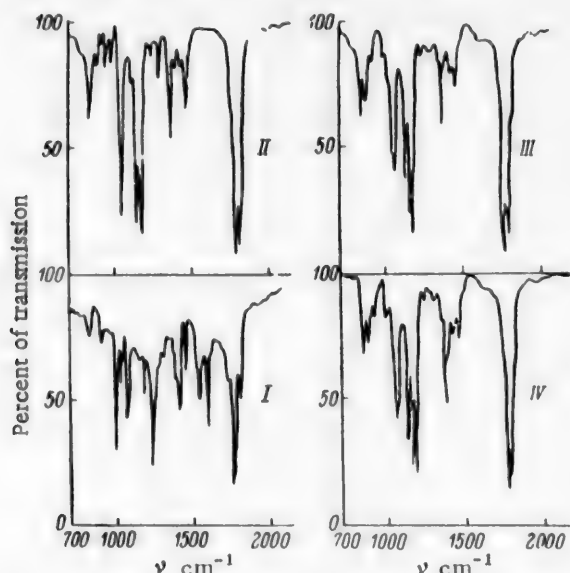


Fig. 2. Infrared transmission spectra of organic peroxides: I) Monochloroacetylbenzoyl; II) acetylisovaleryl; III and IV) acetyl-n-butyryl (explanation in text).

In all the spectra of aromatic peroxides a very intense absorption band is observed in the $1220\text{--}1260\text{ cm}^{-1}$. It is absent in the spectra of solutions of the initial aldehydes and anhydrides. It may be assumed that this band and the $1000\text{--}1030\text{ cm}^{-1}$ band are characteristic of vibrations of a chain of the C—O—C type of the given class of compounds.

The vibrations of such a chain in aliphatic peroxides are probably due to the appearance of bands at 1060 and $1145\text{--}1160\text{ cm}^{-1}$. For peroxides 2, 6, 10, 11, 14 and 13 there are weak absorption bands in the $1300\text{--}1480\text{ cm}^{-1}$ region, with maxima at $1350\text{--}1370$, $1440\text{--}1450$ and $1460\text{--}1470\text{ cm}^{-1}$, which are also observed in the spectra of the initial aldehydes and anhydrides and may be attributed to symmetrical and unsymmetrical deformation vibrations of the C—CH₃ and CH₂ groups. For peroxide 12 (Fig. 2, curve I) in this region of the spectrum there are three absorption bands with maxima at 1415 , 1450 and 1547 cm^{-1} , the interpretation of which is difficult on existing experimental data. In all the spectra of the aromatic peroxides there is a weak band at $1575\text{--}1630\text{ cm}^{-1}$. It is present in the spectra of all the initial aldehydes. Although small, the position of its maximum varies in relation to the position of the substituent in the ring. It must be attributed to vibrations of the benzene ring. Two intense bands in the $1750\text{--}1820\text{ cm}^{-1}$ region are present in the spectra of all these peroxides and are due to C=O vibrations. They are considered characteristic of the given class of compounds. The difference between the maxima of the bands in the spectrum is about

30-38 cm^{-1} . These results agree satisfactorily with the data of [13]. For monochloroacetylbenzoyl peroxide (Fig. 2, curve I) the intensity of the band with a maximum at 1808 cm^{-1} falls markedly, which indicates the considerable effect of the chlorine atom on the vibrations of the neighboring carbonyl group.

Fig. 2 (curves III and IV) gives the spectra of acetyl-n-butyryl peroxide obtained respectively by oxidation of n-butyric aldehyde in acetic anhydride and acetylation of perbutyric acid by acetic anhydride. Their spectra are identical.

EXPERIMENTAL

Initial substances. The acetic anhydride was kept over sodium and distilled directly before the experiment; the b.p. was 137-139°, n_D^{20} was 1.3900. Propionic anhydride was obtained by distillation of propionic acid with acetic anhydride [14], the b.p. was 166-167°, n_D^{20} was 1.4045. Monochloroacetic anhydride was obtained by slow distillation of monochloroacetic acid over P_2O_5 in vacuum [15]; the m.p. was 49°. n-Butyric anhydride was obtained by distillation of n-butyric acid and acetic anhydride [16], the b.p. was 187-191°, n_D^{20} was 1.4125. The benzaldehyde was distilled directly before the experiment; the b.p. was 51° at 5 mm, n_D^{20} was 1.5463. o-Methylbenzaldehyde was obtained by oxidation of o-xylene by chromyl chloride [17]; the b.p. was 49° at 2 mm, n_D^{20} was 1.5482. m-Methylbenzaldehyde was obtained similarly from m-xylene [17]; the b.p. was 81-82° at 13 mm, n_D^{20} was 1.5418. p-Methylbenzaldehyde was obtained by the Gattermann-Koch reaction [18] from toluene; the b.p. was 201-203°, n_D^{20} was 1.5470. 2,4-Dimethylbenzaldehyde was obtained in a similar way to p-methylbenzaldehyde from m-xylene [18]; the b.p. was 63-64° at 2 mm; n_D^{20} was 1.5495. p-Methoxybenzaldehyde was distilled directly before the experiment; the b.p. was 101.5° at 5 mm, n_D^{20} was 1.5762. o-Chlorobenzaldehyde was obtained from o-chlorotoluene by chlorination, followed by saponification of o-chlorobenzylidene chloride by sulfuric acid [19]; the b.p. was 93° at 13 mm, n_D^{20} was 1.5670. m-Chlorobenzaldehyde was obtained by reducing m-nitrobenzaldehyde to m-aminobenzaldehyde, followed by diazotization of the latter [20]; the b.p. was 81-83° at 7 mm, n_D^{25} was 1.5633. p-Chlorobenzaldehyde was obtained by chlorination of p-chlorotoluene, followed by saponification of p-chlorobenzylidene chloride with sulfuric acid [21]; the m.p. was 47°. n-Butyric aldehyde was distilled in a fractionating column; the b.p. was 75.5°, n_D^{20} was 1.3831. Isovaleric acid was distilled twice with an efficient fractionating column; the b.p. was 92°, n_D^{21} was 1.3895. Perbutyric acid was obtained from n-butyric acid and 92% hydrogen peroxide [22]; the b.p. was 27-32.5° at 13 mm; n_D^{20} was 1.4138.

Experimental procedure. The peroxides were obtained by oxidation of o-methylbenzaldehyde, 2,4-dimethylbenzaldehyde, p-methoxybenzaldehyde, m-chlorobenzaldehyde and p-chlorobenzaldehyde in the anhydride of the acid by air in the presence of anhydrous sodium acetate (0.1-0.2%) in an apparatus similar to that described in [6]. The aldehyde : anhydride molar ratio varied with wide limits (from 1 : 1.2 to 1 : 4). The air velocity varied from 0.25 to 1.5 liters per minute. The accumulation of peroxide in the reaction mixture was determined iodometrically [23] by taking samples periodically at intervals of 1-2 hours, depending on the rate of oxidation. The oxidation of m-methylbenzaldehyde, p-methylbenzaldehyde, o-chlorobenzaldehyde, m-chlorobenzaldehyde, benzaldehyde, n-butyric and isovaleric aldehyde was carried out in a sealed vessel by oxygen, the reaction mixture being mixed by a magnetic stirrer. The reaction was carried out until absorption of oxygen had ceased. The reaction mixture was poured into cold water and left for a day, the aqueous layer was decanted, the residue was dissolved in ether, the ether solution was washed with a dilute solution of sodium bicarbonate, and with water, and was then dried over sodium sulfate. After the ether had been distilled, the residue was weighed and its peroxide content was determined. The peroxide yield was calculated, on the basis of 100%.

The results of the experiments are given in the table.

For purification, peroxides 1, 3, 9, 10 and 11 were also treated with nitric acid (1 : 1) for 25-30 minutes, poured into cold water, extracted with ether, washed with a dilute solution of alkali (5%), and with water and then dried over sodium sulfate. Peroxides 2, 3, 5, 7 and 8 were purified by recrystallization from petroleum ether; peroxide 12 was frozen at -70° from a mixture of petroleum ether and ethyl ether (1 : 1).

To confirm the structure of peroxide 13, it was obtained by acetylation of perbutyric acid. 3.00 g of acetic anhydride was added dropwise at the usual temperature to 2.00 g of perbutyric acid (82%). After 12 hours, water was added to the mixture at room temperature to hydrolyze the anhydride; the peroxide was then extracted with ether, washed with dilute sodium bicarbonate and dried over sodium sulfate. After the ether had been distilled under vacuum we obtained 1.66 g (63.7%) of 90.0% acetyl-n-butyryl peroxide. The peroxide content in the sample after distillation under vacuum was 96.8%; the b.p. was 37-41° (2 mm), n_D^{20} was 1.4131.

Serial No.	Name of aldehyde	Amount (in g-mole)	Amount of anhydride (in g-mole)	Expt. temp.	Reaction time (in hours)	Peroxides obtained	Melting point	Boiling point (pres- sure in mm)	n_D^{20}	n_D^{20}	Molecular weight found	Molecular weight calcu- lated	% of peroxide	Percentage Yield
1	o-Methylbenzoic	0.025	0.117	45°	3	Acetyl-o-methylbenzoyl	—	—	1.1620	1.5126	185	194	96.8	81.4
2	m-Methylbenzoic	0.020	0.070	50	4	Acetyl-m-methylbenzoyl	32.0— 32.5°	—	—	—	187	194	99.6	78.0
3	p-Methylbenzoic	0.017	0.039	40	4	Acetyl-p-methylbenzoyl	65.0— 65.5	—	—	—	187	194	99.5	74.9
4	2,4-Dimethylbenzoic	0.022	0.147	40	5.5	Acetyl-2,4-dimethyl- benzoyl	—	—	1.1376	1.5216	196	208	92.6	73.6
5	p-Methoxybenzoic	0.068	0.210	30	12	Acetyl-p-methoxybenzoyl	59.5	—	—	—	190	210	96.5	63.0
6	o-Chlorobenzoic	0.036	0.106	40	4	Acetyl-o-chlorobenzoyl	—	—	1.2589	1.5305	182	214.5	90.5	81.5
7	m-Chlorobenzoic	0.054	0.210	40	10	Acetyl-m-chlorobenzoyl	53.0— 54.0	—	—	—	198	214.5	96.0	92.5
8	p-Chlorobenzoic	0.018	0.150	40	5	Acetyl-p-chlorobenzoyl	49.5	—	—	—	208	214.5	99.7	83.0
9	Benzoic	0.056	0.110	40	5	Propionylbenzoyl	—	—	1.1530	1.5097	181	194	97.0	79.0
10	m-Chlorobenzoic	0.060	0.120	40	6	Propionyl-m-chloro- benzoyl	—	—	1.2222	1.5170	208	228	92.0	81.5
11	Benzoic	0.034	0.070	40	12	n-Butylbenzoyl	—	—	1.0671	1.5040	180	208	95.0	83.0
12	Benzoic	0.040	0.090	50	5	Monochloroacetylbenzoyl	—	—	1.2386	1.5313	—	—	98.0	78.0
13	n-Butyric	0.050	0.100	20—25	4	Acetyl-n-butyryl	—	37— 37.5° (2)	1.0610	1.4123	138	146	98.3	81.1
14	Isovaleric	0.050	0.105	20—25	3	Acetylisovaleryl	—	40— 41.5 (2)	1.0260	1.4145	152	160	96.0	75.5

• Peroxides 1-8, 13 and 14 were obtained by oxidation of the corresponding aldehydes in acetic anhydride; peroxides 9 and 10 were obtained in propionic anhydride; peroxide 11 in n-butyric anhydride; peroxide 12 in monochloroacetic anhydride.

SUMMARY

1. A new method was developed for the synthesis of unsymmetrical diacyl peroxides by oxidation of aldehydes in the presence of acid anhydrides.

2. The following unsymmetrical diacyl peroxides were obtained for the first time: acetyl-n-butyryl, acetyl-isovaleryl, acetyl-o-methylbenzoyl, acetyl-m-methylbenzoyl, acetyl-p-methylbenzoyl, acetyl-2,4-dimethylbenzoyl, acetyl-p-methoxybenzoyl, acetyl-o-chlorobenzoyl, acetyl-m-chlorobenzoyl, acetyl-p-chlorobenzoyl, propionyl-benzoyl, propionyl-m-chlorobenzoyl, n-butyrylbenzoyl and monochloroacetylbenzoyl. Their physicochemical constants were described and their infrared spectra are investigated and interpreted.

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THE REDUCTION OF NAPHTHOL CARBOXYLIC ACIDS

VI. PREPARATION OF THE METHYL ESTER OF 2,1-TETRALONE

CARBOXYLIC ACID

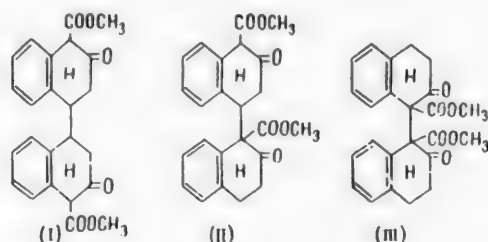
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Original article submitted September 13, 1960

Esters of 2,1-tetralone carboxylic acid until recently have been compounds which were very difficult to obtain. For example, a recently described process for preparing the ethyl ester of this β -ketoacid consists of a rather complex conversion from 2,3-naphthol carboxylic acid to o-phenyleneacetopropionic acid with later cyclization of its diester by the Dieckmann reaction [1]. The simple method which we have found for preparing 2,1-tetralone carboxylic acid [2] opens a new, more suitable path for preparative synthesis of the methyl ester of this ketoacid, which can be used in organic syntheses for various purposes.

For conversion of 2,1-tetralone carboxylic acid into its methyl ester we used the results which we obtained earlier in solving the analogous problem for 2,3-tetralone carboxylic acid [3]. However, considering the especially great tendency of this β -ketoacid to undergo decarboxylation, which makes its isolation and purification very difficult, we submitted directly to the action of an ether solution of diazomethane a mixture of substances extracted by ether from the acidified reaction mass obtained by indirect electroreduction of 2,1-naphthol carboxylic acid. In the first experiments we carried out the reduction process under exactly the same conditions as were used previously [2]. After the corresponding treatment we succeeded in isolating the methyl ester of 2,1-tetralone carboxylic acid with a yield of only about 20% (on the starting 2,1-naphthol carboxyl), since part of the β -ketoacid formed in the reduction was converted into β -tetralone (yield 22%). The total yield of methyl ester and β -tetralone was 40-45% on the hydroxynaphthoic acid.

The methyl ester of 2,1-tetralone carboxylic acid was a viscous liquid. We also isolated from the reaction mixture obtained after methylation a white, crystalline substance with m.p. 205-210° which had almost the same composition as the methyl ester of 2,1-tetralonecarboxylic acid, but twice the molecular weight. This compound, which had the properties of a β -ketoester, was certainly the dimethyl ester of one of the three di(β -tetralone carboxylic acids) (I-III) the formation of which in the reaction of indirect electroreduction of 2,1-naphthol carboxylic acid was recently established by us [2]:



Ketonic splitting of this diester led to the di- β -tetralone with m.p. 272° described by us in the work mentioned above [2]. The yield of diketodiester was 11-14%.

We did not isolate the two other possible isomers of the diketodiester although the large residue after distillation of the methyl ester of 2,1-tetralone carboxylic acid indicates the probability of the presence of these dimeric products.

To raise the yield of the ester of 2,1-tetralone carboxylic acid we decreased the concentration of the 2,1-naphthol carboxylic acid in the indirect electroreduction. Corresponding with the earlier noted regularities [4] of the dependence of the yield of reductive dimerization product on concentration of reduced substance, the yield of diester of diketodiacid in methylation of the reaction mixture was in this case only about 4%, while the yield of methyl ester of 2,1-tetralone carboxylic acid reached 30%, and the total yield of this ester and β -tetralone was 60%, calculated on the starting 2,1-naphthol carboxylic acid.

EXPERIMENTAL

1. Reduction of 2,1-naphthol carboxylic acid.* Twenty g of 2,1-naphthol carboxylic acid was dissolved in soda solution (20 g of Na_2CO_3 in 300 ml of water), 40 g of boric acid was added and the solution was cooled to 0°. We placed 150 ml of water and 150 g of ice chips in the electrolyzer [5], applied a current strength of 5 A and after 15 minutes began slow addition through a dropping funnel of the above solution of 2,1-naphthol carboxylic acid. The gradual addition of the solution (about two hours) assured a small concentration of naphthol carboxylic acid during the entire period of the reaction. The reaction mixture was kept at a pH of 7.0-8.0 by passage of CO_2 and the vessel was cooled to the range 5-6°. After the addition of the whole solution of naphthol carboxylic acid under the same conditions it was stirred for about one hour more, so that the total duration was 3.5 hours.

2. Methylation of the reduction products. The solution of the reduction products of 2,1-naphthol carboxylic acid obtained by the above process was transferred to a beaker, cooled to 0°, and carefully acidified with a 10% sulfuric acid solution, previously cooled to 0°. The precipitate which separated was dissolved in ether, which was washed with cold water, cooled to 0° and treated with an ether solution of diazomethane obtained from 25 g of nitrosomethylurea [6]. The reaction mixture stood overnight in the refrigerator. The precipitate of diester of diketodicarboxylic acid (0.2 g, decomposition point 195-200°) was filtered off, and the ether solution was washed with 10% acetic acid to decompose the remaining diazomethane, then with water, with a solution of sodium bicarbonate, and again with water. After drying with sodium sulfate and distillation of the solvent, we obtained an oily residue from which we isolated a further 0.7 g of diester of diketodicarboxylic acid (total yield about 4%). The product separated from the diester (about 19 g) was distilled in a vacuum. In the fraction with b.p. 105-140° (4 mm) we collected a mixture of methyl ester of 2,1-tetralone carboxylic acid and β -tetralone (13.1 g).

a) Methyl ester of 2,1-tetralone carboxylic acid. This fraction (13.1 g) was dissolved in 70 ml of benzene and cooled to -3°; the solution was washed three times with a solution of 5% potassium hydroxide, also cooled. The alkaline extract (cooled) was acidified with a cooled 10% acetic acid solution. The oily product which precipitated was extracted three times with ether; the combined ether extracts were washed successively with water, a bicarbonate solution, and water. After drying with sodium sulfate and distillation of the solvent, the residue (about 8 g) was distilled in a vacuum. We obtained 6.4 g with b.p. 126° (2 mm), n_D^{20} 1.5820, d_4^{20} 1.2019.

Found %: C 70.30, 70.18; H 5.82, 5.65. $\text{C}_{22}\text{H}_{12}\text{O}_3$. Calculated %: C 70.57; H 5.92.

Yield 30%, calculated on 2,1-naphthol carboxylic acid.

The copper salt was obtained by the action of 5% aqueous methanol (1 : 1) solution of copper acetate (15 ml) on a methanol solution of the ketoester (1 g in 5 ml). After two days crystals formed. After recrystallization from methanol, glittering plates of a light brown color, m.p. 216-218°.

Found %: C 61.22, 61.30; H 5.59, 5.55; CuO 17.26. $(\text{C}_{22}\text{H}_{11}\text{O}_3)_2\text{Cu}$. Calculated %: C 61.34; H 4.72; CuO 16.91.

2,4-Dinitrophenylhydrazone, orange crystals, m.p. 194-196° (from a mixture of alcohol and ethyl acetate).

Found %: N 13.96, 14.09. $\text{C}_{18}\text{H}_{16}\text{O}_6\text{N}_4$. Calculated %: N 14.58.

b) β -Tetralone. The benzene solution after removal of the alkaline ketoester from it was washed with acetic acid, then with water, a solution of sodium bicarbonate, and with water, and dried over sodium sulfate. After distillation of the solvent the residue was distilled in a vacuum. The fraction with b.p. 95-100° (2 mm), n_D^{20} 1.5593 was 4.32 g (29%). Literature data [7].

c) Dimethyl ester of di(2,1-tetralone carboxylic acid). For isolation, see above. If we carry out the reduction of 2,1-naphthol carboxylic acid under conditions described previously [2], the yield is 11-14%, against 4% ob-

* We give the conditions at which formation of the products of reductive dimerization is at a minimum.

tained by the present method. Poorly soluble in alcohol, acetone, and benzene. Dissolves in 5% KOH solution. Gives a blue-green color in an alcoholic FeCl_3 solution. M.p. 205-210° (from dioxane).

Found %: C 70.97, 70.82; H 5.11, 5.20; ester number 279. M 357. $\text{C}_{24}\text{H}_{22}\text{O}_6$. Calculated %: C 70.92; H 5.45; ester number 276. M 406.

The diketoester was acetylated under the usual conditions and gave results which corresponded to a compound with two hydroxyl groups.

Found %: OH 8.6. Calculated %: OH 8.36.

Ketonic decomposition. One g of diketoester was dissolved with careful heating in 15 ml of 5% KOH solution, then boiled for 15 minutes. The precipitate which formed (0.46 g) had m.p. 270°. After recrystallization from dioxane, m.p. 272-273°. A sample mixed with diketone A obtained by indirect electroreduction of 2,1-naphthol carboxylic acid [2] showed no melting point depression.

SUMMARY

1. We have worked out a method for preparing the methyl ester of 2,1-tetralone carboxylic acid by the action of diazomethane on the mixture of products of reduction of 2,1-naphthol carboxylic acid. Along with this ketoacid there is also formed the dimethyl ester of di(2,1-tetralone carboxylic acid).

2. We have shown that the greatest yield of ester of 2,1-tetralone carboxylic acid (30%), and the minimum yield of products of reductive dimerization is obtained by reduction of a very dilute solution of 2,1-naphthol carboxylic acid.

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SYNTHESIS AND STUDY OF HETEROCYCLIC
DERIVATIVES WITH POTENTIAL ANTICANCER
ACTIVITY

I. SOME DERIVATIVES OF *m*-PHENANTHROLINE

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Among the organic compounds studied in recent years as anticancer substances the so-called alkylating compounds and antimetabolites are very interesting [1].

Among the alkylating compounds some bis- β -chloroethylamines have found practical use in the chemotherapy of various types of tumors and tumorous processes of the hemopoietic system (embichine, novoembichine, nitromine, dopane, and others). Among the bis- β -chloroethylamines which contain heterocyclic radicals, derivatives of furan [2], thiophene [3], benzimidazole [4-8], pyrimidine [9-12], pyrene [13-14], quinoline [15-16], acridine [15] and others have been studied. Among the antimetabolites of protein metabolism (amino acid antagonists) there were synthesized heterocyclic analogs of unsubstituted amino acids, especially β -phenyl- α -alanine, for example, 2-, 3-, and 4-pyridylalanine [17-18], 2-quinolylalanine [19], 2-thienylalanine [20], 5-cytosylalanine [21], and others.

In the present work we have described the synthesis of two derivatives of *m*-phenanthroline intended for biological study; one of them belongs to the alkylating substances: 6-[bis(β -chloroethyl)aminomethyl]-1,7-phenanthroline (VI), and the second is a heterocyclic analog of phenylalanine: β -[6-(1,7-phenanthrolyl)]- α -alanine (VIII). As the basis for preparing the *m*-phenanthroline derivatives we considered first that even the unsubstituted *o*-, *m*-, and *p*-phenanthrolines are active against sarcoma 37 [22], and second, that many derivatives of phenanthroline have different physiological activities (carcinolytic [23] etc.).

6-Methyl-1,7-phenanthroline (Ia) was obtained by the Skraup reaction [24] from 2,4-toluylenediamine; as the oxidizing agent we used picric acid or arsenic anhydride. Isolation and purification of the product were carried out through the difficultly soluble salt with chromic acid [25]. Yield 30%. By bromination of methylphenanthroline with bromosuccinimide in the presence of benzoyl peroxide we obtained 6-bromomethyl-1,7-phenanthroline (II). The action of diethanolamine on the bromoderivative (II) gave a condensation product as the hydrobromide (III) from which we isolated 6-[bis(β -hydroxyethyl)aminomethyl]-1,7-phenanthroline (IV) in the form of a low melting, hygroscopic oil which gave a hydrochloride with m.p. 211-212° (from anhydrous alcohol). When we boiled the free base (IV) or its hydrochloride with thionyl chloride we formed the hydrochloride of 6-[bis(β -chloroethyl)aminomethyl]-1,7-phenanthroline (V), from which by the action of dilute alkali we isolated the free base (VI). On treatment of the bromomethyl derivative (II) with sodium-(acetylamino)malonic ester in alcohol we obtained a condensation product (VII) whose hydrolysis gave β -[6-(1,7-phenanthrolyl)]- α -alanine (VIII) which gave a positive ninhydrin reaction.

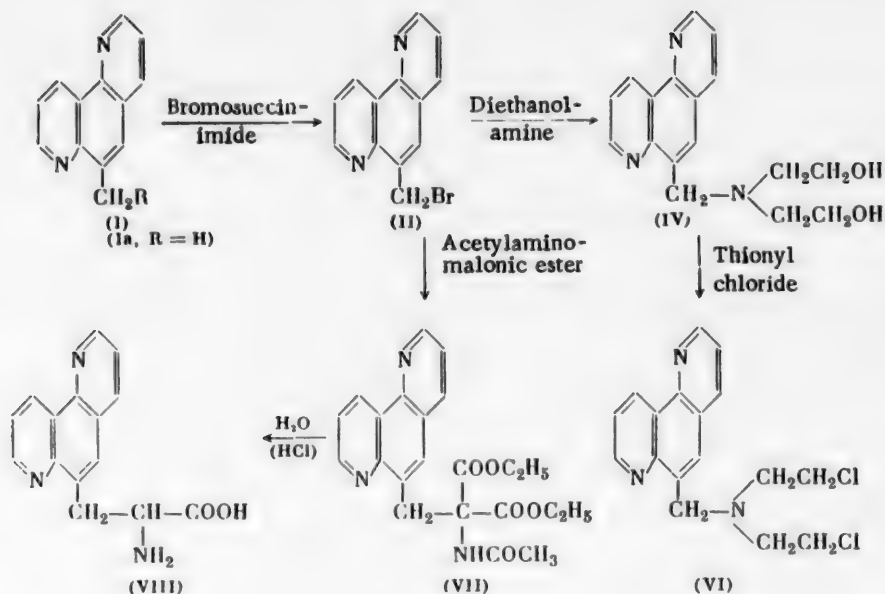
A brief report of the characteristics of the products with the general formula (I) is given in the table.

EXPERIMENTAL*

6-Bromomethyl-1,7-phenanthroline (II). We placed in a flask 9.7 g of (Ia), 8.8 g of bromosuccinimide, 0.54 g of benzoyl peroxide, and 100 ml of carbon tetrachloride, boiled the mixture for two hours, cooled, and filtered off the succinimide. The solvent was distilled off and the somewhat oily residue was washed with a weak solution of

* G. A. Nudel' took part in the experiments.

Synthesis of substances (VI) and (VII) is shown in the scheme:



alkali and with water. The dried precipitate was recrystallized from ligroin. We obtained colorless crystals with m.p. 127.5-128.5°. Yield 6.9 g (50.5%).

6-[Bis(β-hydroxyethyl)aminomethyl]-1,7-phenanthroline (hydrobromide) (III). We placed in a flask 5.5 g of (II), 2.1 g of diethanolamine, and 40 ml of butyl alcohol, boiled the mixture for one hour, cooled, and filtered off the crystalline product which we recrystallized from butyl alcohol. We obtained colorless crystals with m.p. 203-203.5°. Yield 5.7 g (75%).

6-[Bis(β-chloroethyl)aminomethyl]-1,7-phenanthroline (VI). We dissolved 3.78 g of (III) in a small amount of water, made it alkaline with 40% alkali solution, and extracted the oil which precipitated with chloroform. The extract, dried over anhydrous sodium sulfate, was treated with 18 ml of thionyl chloride with cooling, and was boiled for two hours. After cooling, the slightly yellowish crystalline product (V) was filtered, washed with chloroform, placed in ice water, and treated with a dilute alkali solution. The oil which separated crystallized in a cooler and was filtered, washed, and dried over phosphorus pentoxide. After crystallization from ligroin with addition of anhydrous alcohol we obtained colorless crystals (slightly hygroscopic) with m.p. 85-85.5°. Yield of (VI) 1.5 g (45%). One g of (VI) was dissolved in anhydrous alcohol and dry hydrogen chloride was passed in. The hydrochloride (V) precipitated and was filtered off, washed with anhydrous alcohol, and dried; m.p. 250-251° (with decomposition). Yield 1 g (82%).

Ethyl ester of β-[6-(1,7-phenanthrolyl)-α-(carbethoxy)-α-N-acetylamino]propionic acid (VII). In a three-necked round bottomed flask with a condenser and stirrer we placed 60 ml of anhydrous alcohol, added 0.1 g of sodium in small pieces, and after solution of the latter, 8.7 g of acetylamino-malonic ester. The mixture was boiled for 15 minutes cooled, and 10.84 g of (II) was added. After boiling for two hours, the contents of the flask were cooled, diluted with 200 ml of water; the oil which then separated crystallized. After crystallization from 30% aqueous alcohol we obtained colorless crystals with m.p. 146.5-147.5° (VII). Yield 5.65 g (34.4%).

β-[6-(1,7-phenanthrolyl)]-α-alanine (VIII). A mixture of 5.65 g of (V) and 50 ml of 20% hydrochloric acid was boiled for three hours, cooled, and neutralized with aqueous ammonia to pH 7. After crystallization the precipitate was filtered off, washed, and recrystallized from water; we obtained colorless crystals with m.p. 263.5-264.5°. Yield 0.6 g (16.3%).

SUMMARY

We have prepared for biological study 6-[bis(β-chloroethyl)aminomethyl]-1,7-phenanthroline and β-[6-(1,7-phenanthrolyl)]-α-alanine.

Properties of Substances with the General Formula



Compound	R	M. p.	Yield %	Empirical formula	% C		% H		% N		% Halogen	
					found	calcu- lated	found	calcu- lated	found	calcu- lated	found	calcu- lated
(II)	Br	127.5—128.5°	50.5	$C_{13}H_9N_2Br$	57.64	57.14	3.12	3.30	10.56, 10.02	10.26	28.30	29.30
(III)	$N \begin{smallmatrix} \text{CH}_3\text{CH}_2\text{OH} \\ \text{CH}_3\text{CH}_2\text{OH} \end{smallmatrix} \cdot HBr$	203—203.5	75	$C_{17}H_{19}O_2N_3 \cdot HBr$	—	—	—	—	11.11, 11.00	11.11	21.53	21.17
(V)	$N \begin{smallmatrix} \text{CH}_3\text{CH}_2\text{Cl} \\ \text{CH}_3\text{CH}_2\text{Cl} \end{smallmatrix} \cdot 2HCl$	250—251	82	$C_{17}H_{17}N_3Cl_2 \cdot 2HCl$	49.81, 49.78	50.12	4.60, 4.52	4.66	10.56, 10.31	10.32	35.05	34.88
(VI)	$N \begin{smallmatrix} \text{CH}_3\text{CH}_2\text{Cl} \\ \text{CH}_3\text{CH}_2\text{Cl} \end{smallmatrix}$	85—85.5	45	$C_{17}H_{17}N_3Cl_2$	61.30	61.07	4.80	5.09	12.68	12.54	21.23	21.25
(VII)	$\begin{smallmatrix} \text{COOC}_2\text{H}_5 \\ \text{C} \begin{smallmatrix} \text{COOC}_2\text{H}_5 \\ \text{NHCOCH}_3 \end{smallmatrix} \end{smallmatrix}$	146.5—147.5	34.4	$C_{22}H_{23}O_5N_3$	64.83, 65.01	64.54	5.94, 5.98	5.62	10.28, 10.24	10.02	—	—
(VII)	$\begin{smallmatrix} \text{CH-COOH} \\ \\ \text{NH}_2 \end{smallmatrix}$	263.5—264.5	16.3	$C_{15}H_{13}O_2N_3$	67.59, 67.59	67.41	4.88, 4.90	4.87	15.77, 15.73	15.73	—	—

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THE SYNTHESIS OF SUBSTANCES WHICH CONTAIN
FRAGMENTS OF FOLIC ACID

II. THE DIPEPTIDE OF THE DIETHYL ESTER OF d,l-GLUTAMIC ACID
AND β -[p-BIS(β' -CHLOROETHYL)AMINOPHENYL]- α -ALANINE

L. V. Alekseeva and Z. V. Pushkareva

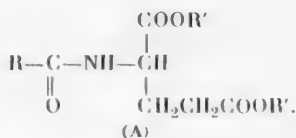
S. M. Kirov Ural Polytechnic Institute

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Original article submitted August 25, 1960

In the previous communication [1] we described the synthesis of a series of N-acyl derivatives of d,l-glutamic acid with the general formula (A)



In the present work we describe N-acyl derivatives of the diethyl ester of d,l-glutamic acid which contain residues of a molecule with known anticancer activity, p-bis(β -chloroethyl)aminophenylalanine (sarcocysine).

In recent years a series of dipeptides of sarcocysine with various amino acids have been prepared and studied, and some of them show valuable anticancer properties [2, 3].

The diethyl ester of N'-[p-bis(β -chloroethyl)aminophenyl-N-acetylalanyl]-d,l-glutamic acid (I) was prepared by condensation of N-acetylsarcocysine [4] with the diethyl ester of d,l-glutamic acid in the presence of 1,3-dicyclohexylcarbodiimide. As a result of the reaction we obtained a crystalline substance from which by repeated recrystallizations we obtained two individual products (m.p. 147-148° and m.p. 121-122°), in approximately equal amounts. Both products were optically inactive, had the same composition, and differed considerably in solubility. Probably these substances are racemates of diastereoisomeric dipeptide (I). The condensation product can also be isolated in the form of a hydrochloride which, however, could not be separated into two substances.

The diethyl ester of N'-[p-bis(β -chloroethyl)aminophenyl-N-formylalanyl]-d,l-glutamic acid (III) is formed by condensation of N-formylsarcocysine [4] with the diethyl ester of d,l-glutamic acid in the presence of 1,3-dicyclohexylcarbodiimide.

On hydrolysis of the formyl portion of ester (III) with an alcoholic solution of HCl we obtained the dihydrochloride of the diethyl ester of N'-[p-bis(β -chloroethyl)aminophenylalanyl]-d,l-glutamic acid (IV).

Because of the instability of the dihydrochloride of dipeptide (IV) the latter was obtained in the form of the salt with methylene-di(β -hydroxynaphthoic acid) (V).

The properties of the compounds which were synthesized are given in the table.

EXPERIMENTAL

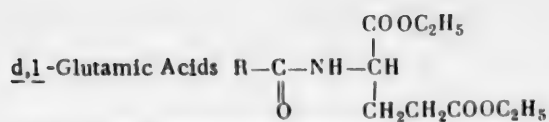
Diethyl ester of N'-[p-bis(β -chloroethyl)aminophenyl-d,l-N-acetylalanyl]-d,l-glutamic acid (I). To a suspension of 2.5 g of N-acetylsarcocysine in 10 ml of anhydrous chloroform we added 1.4 g of 1,3-dicyclohexylcarbodiimide in 5 ml of chloroform. The mixture was energetically shaken and left overnight at room temperature. The precipitate of dicyclohexylurea was filtered off, the filtrate was evaporated and the remaining oil slowly crystallized on the addition of a small amount of alcohol and cooling. The resulting precipitate was filtered off, yield 1.2 g

Dipeptides of Diethyl Esters of

Substance No.	R	M. p.	Yield, %
(I)		a) 147–148° b) 121–122°	21
(II)		79–80	74–75
(III)		70–71	55–60
(IV)		63–65	75–78
(V)		96–98 (decomp)	70–78

(21%), m.p. 130–132°. On recrystallization from a mixture of anhydrous alcohol and ligroin (1 : 1) two products were separated from it: one poorly soluble in this mixture (0.6 g) with m.p. 147–148° (from alcohol) and one easily soluble (0.55 g) with m.p. 121–122° (from alcohol).

Hydrochloride of diethyl ester of N'-[p-bis(β-chloroethyl)aminophenyl-N-acetylalanyl]-d,l-glutamic acid (II). The oily product obtained as a result of evaporation of the solvent after carrying out the condensation reaction by the method given above was dissolved in 5 ml of anhydrous alcohol, and dry hydrogen chloride was passed into the solution with cooling; the solution decolorized with activated charcoal and poured into 50 ml of absolute ether. The



Empirical formula	% C		% H		% N	
	found	calculated	found	calculated	found	calculated
$\text{C}_{24}\text{H}_{35}\text{O}_6\text{N}_3\text{Cl}_2$	54.16, 54.17	54.14	6.54, 6.58	6.58	7.98, 7.94	7.89
$\text{C}_{24}\text{H}_{36}\text{O}_6\text{N}_3\text{Cl}_3$	50.69, 50.82	50.66	6.30, 6.25	6.33	7.51, 7.54	7.38
$\text{C}_{23}\text{H}_{33}\text{O}_6\text{N}_3\text{Cl}_2$	53.42, 53.38	53.28	6.30, 6.42	6.37	8.24	8.11
$\text{C}_{22}\text{H}_{35}\text{O}_5\text{N}_3\text{Cl}_4$	46.78, 46.99	46.89	6.31, 6.30	6.22	7.62, 7.54	7.46
$\text{C}_{22}\text{H}_{35}\text{O}_5\text{N}_3\text{Cl}_2 \cdot 0.5 (\text{C}_{23}\text{H}_{16}\text{O}_6)$	58.93, 58.90	58.77	5.99, 6.02	5.99	6.37, 6.13	6.14

resulting white crystalline precipitate was purified by reprecipitation from alcohol solution by ether. We obtained 4.2 g of a hygroscopic substance which decomposed in the light.

Diethyl ester of N'-[p-bis(β-chloroethyl)aminophenyl]-N-formylalanyl]-d,l-glutamic acid (III). We dissolved 1.2 g of the hydrochloride of the diethyl ester of d,l-glutamic acid in 5 ml of anhydrous alcohol and added to the solution with cooling 0.7 ml of triethylamine in 25 ml of absolute ether. The precipitate of triethylamine hydrochloride was filtered off. To the filtrate we added 1.65 g of N-formylsarcosine and 1.032 g of 1,3-dicyclohexylcarbodiimide in 5 ml of chloroform. The mixture was shaken energetically and left overnight at room temperature. The precipitate of dicyclohexylurea was filtered off, and the filtrate was evaporated. The remaining oil crystallized on long standing in a refrigerator. Yield 1.6 g.

Dihydrochloride of the diethyl ester of N-[p-bis(β -chloroethyl)aminophenylalanyl]-d,l-glutamic acid (IV). We dissolved 1.4 g of the diethyl ester of N'-[p-bis(β -chloroethyl)aminophenyl-N-formylalanyl]-d,l-glutamic acid in 17 ml of 6 N alcoholic solution of HCl, boiled the solution for 1 minute and then evaporated in a vacuum to a volume of 5 ml and poured it into 50 ml of absolute ether. The white crystalline precipitate was purified by reprecipitation from alcohol solution by absolute ether. The product was hygroscopic and became rose colored on standing in the light.

Salt of diethyl ester of N-[p-bis(β -chloroethyl)aminophenylalanyl]-d,l-glutamic acid and methylene-di(β -hydroxynaphthoic acid) (V). We shook 1.2 g of the dihydrochloride of the diethyl ester of N-[p-bis(β -chloroethyl)aminophenylalanyl]-d,l-glutamic acid energetically with a mixture of 20 ml of 10% sodium bicarbonate solution and 20 ml of ether to disappearance of the precipitate. The ether layer was separated, the water was extracted with ether, the ether extracts were dried with sodium sulfate. The oil which remained after distillation of the ether was dissolved in 3 ml of dry tetrahydrofuran and to the solution was added 0.4 g of methylene-di(β -hydroxynaphthoic acid); the mixture was brought to boiling and the insoluble precipitate was filtered off. The filtrate was poured by drops into ice water. The flakey precipitate was filtered off and dried. Purification was carried out by reprecipitation from tetrahydrofuran with water and from alcohol with water.

SUMMARY

We have synthesized for biological study the diethyl ester of N'-[bis(β -chloroethyl)aminophenyl-N-acetylalanyl]-d,l-glutamic acid and the salt of the diethyl ester of N-[bis(β -chloroethyl)aminophenylalanyl]-d,l-glutamic acid with methylene-di(β -hydroxynaphthoic acid).

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THE SYNTHESIS OF SODIUM TETRAPHENYLBORON IN A TETRAHYDROFURAN MEDIUM

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Original article submitted July 13, 1960

Sodium tetraphenylboron is of interest for analytical chemistry, as a reagent for the potassium ion [1]. A method of synthesis of (I) is described in the literature from sodium tetrafluoroboron and phenyl magnesium bromide in ether solution [1]. Since on a works scale the use of a large amount of ether is not desirable, it is of interest to replace the ether by some less inflammable solvent.

We have shown that tetrahydrofuran can be used for this purpose. However, on simple use of the method of [1], which consists in this, that NaBF_4 is added to a prepared solution of $\text{C}_6\text{H}_5\text{MgBr}$, the formation of (I) in tetrahydrofuran does not occur. (I) is obtained if NaBF_4 is introduced into the reaction mixture before the reaction is ended between magnesium and bromobenzene. In this connection it is necessary to assume that formation of (I) occurs not as a result of reaction between $\text{C}_6\text{H}_5\text{MgBr}$ and NaBF_4 , as obviously occurs in ether solution. Such a difference is perhaps connected with the lower activity of $\text{C}_6\text{H}_5\text{MgBr}$ solvated with tetrahydrofuran, as compared to the same compound solvated with ether, and in the case of the use of tetrahydrofuran as the solvent, NaBF_4 does not react with $\text{C}_6\text{H}_5\text{MgBr}$ but with some intermediate product. As such we can take the free phenyl radical, which is formed either as a result of reaction between magnesium and bromobenzene, or as a result of reaction between the radical $\text{C}_6\text{H}_5\text{Mg}^\cdot$ and bromobenzene.

The method which we have worked out with the use of tetrahydrofuran as the solvent permits synthesis of (I) with yield of the purified product of 30%, calculated on the NaBF_4 . For the synthesis we used technical tetrahydrofuran, and more than half of the tetrahydrofuran used for synthesis and purification of (I) could be regenerated. For identification and determination of the purity of (I) it was advisable to use the molar coefficient of absorption of a water solution of (I) in the region from 220 to 235 $\text{m}\mu$.

EXPERIMENTAL

In a flask we placed 8 g of activated metallic magnesium turnings, 70 ml of technical tetrahydrofuran (dried with anhydrous Na_2SO_4), and 43 g of bromobenzene. The flask was heated to incipient boiling of the tetrahydrofuran, heating was stopped, and a crystal of iodine was thrown into the flask. In about 15-20 minutes, an energetic reaction began. Three to five minutes after disappearance of the iodine color, stirring was begun and 5 g of NaBF_4 was added. In order to avoid a too stormy reaction, we added NaBF_4 gradually. The flask was then cooled, but so carefully that the reaction did not stop. After addition of the NaBF_4 , the energetic reaction continued for another 30 minutes. Then stirring was continued for 7-8 hours at a temperature in the flask of about 40° . The contents of the flask were poured gradually with stirring into 650-700 ml of a saturated NaCl solution and were extracted with tetrahydrofuran (4 portions of 80 ml). The extract was dried with 50 g of anhydrous Na_2SO_4 for 4-5 hours, the tetrahydrofuran was removed by heating in a vacuum on a water bath heated to $50-55^\circ$. This regenerated 60-65% of the tetrahydrofuran used in the synthesis. The pasty crystalline mass which remained in the flask was treated with 180 ml of chloroform, carefully shaken, and the chloroform was sucked off through a glass filter No. 4; the precipitate of sodium tetraphenylboron was washed on the filter with three portions of chloroform of 30 ml each and the chloroform was carefully sucked off of the residue. The precipitate was dried in a vacuum desiccator. Yield of pure product about 3.7 g. From the filtrate after a day there precipitated about one more gram of sodium tetraphenylboron, which was also sucked off.

The total yield of pure product was 30%. In the water solution of the substance there was an intense absorption spectrum in the far ultraviolet region.

The molar coefficient of absorption at different wave lengths has the following values:

Wave length (in m μ)	K λ
220	25600
225	20000
230	17200
235	14700

SUMMARY

1. We have worked out a method for the synthesis of sodium tetraphenylboron using tetrahydrofuran as the solvent.
2. We have measured the ultraviolet spectrum of sodium tetraphenylboron.

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THE CONDENSATION OF 1-(α -FURYL)-3-METHYL-1,3-BUTADIENE WITH MALEIC ANHYDRIDE

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Voronezh Technological Institute

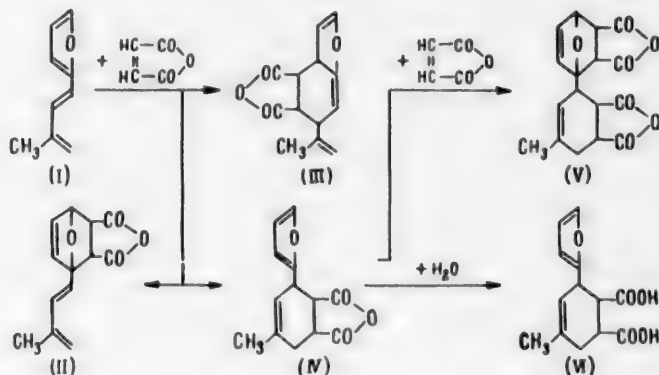
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

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Original article submitted October 17, 1960

In our previous communication [1] we showed that 1-(α -furyl)-3-methyl-1,3-butadiene reacted easily in the diene synthesis with maleic anhydride, and if we used for the reaction a mole ratio of starting substances 1 : 1, there was formed only one crystalline monoadduct whose structure we did not establish.

In the molecule of 1-(α -furyl)-3-methyl-1,3-butadiene (I) are four conjugated double bonds, and therefore the resulting monoadduct can have one of the following structural forms (II, III, IV):



According to the literature, a monoadduct of type (II), formed in the condensation of maleic anhydride with a conjugated system of double bonds of the furan nucleus, is an unstable compound and splits out the starting components not only on heating, but also on long keeping. Monoadducts of types (III) and (IV) are stable substances; on heating with water they are converted into dibasic acids [2-5].

Our monoadduct is a stable compound; it has a sharp melting point and on heating with water is converted into the corresponding dibasic acid. Hence for our monoadduct formula (II) drops out and it remains to choose between formulas (III) and (IV).

In the molecule of possible isomer (III) a conjugated system of double bonds is absent, and in the molecule of isomer (IV) there is a conjugated system in the furan nucleus. In this connection, if the monoadduct obtained under the above conditions has structure (IV), it should react with a second molecule of maleic anhydride with formation of the bisadduct (V).

Experiments showed that the monoadduct reacts at room temperature in acetone solution with a second molecule of maleic anhydride with formation of the bisadduct (V). This shows that at a molar ratio of 1 : 1 maleic anhydride first reacts with the more reactive conjugated system of double bonds of the side chain of (I) with formation of the monoadduct with structural formula (IV).

The bisadduct (V) is also obtained with a good yield if for the condensation at room temperature in absolute ether we take two moles of maleic anhydride for one mole of (I). The bisadduct, as a compound which contains an oxygen endo-bridge, is an unstable substance. Especially in the crude state it turns yellow when kept in air. On

melting, the bisadduct gradually decomposes; the melting point is lower, the more slowly the temperature is raised in the apparatus. Thus, in an ordinary determination of the melting point the bisadduct melts at 101.0-102.0° and 105.0-105.5°; if the bisadduct is heated in a capillary at 85.5-88.0°, after 25 minutes there begins tarring of the crystals, and after 35 minutes, melting begins; after 40 minutes melting of the crystals is complete. When the bisadduct is heated with water, it gradually decomposes into a water soluble substance.

EXPERIMENTAL

1-(α -Furyl)-3-methyl-1,3-butadiene (I) was obtained by dehydration of 1-(α -furyl)-3-methyl-1-buten-3-ol, synthesized by the method described previously [1]. The best yield of (I) was found if dehydration was carried out in a vacuum (20 mm) in the absence of oxygen of the air (nitrogen) with slow addition of the alcohol from a dropping funnel into a Claisen flask with several iodide crystals (0.005-0.01 g), heated on an oil bath to 130-140°. From 38.75 g of alcohol we distilled 20.55 g (53.0%) of dehydration product, from which we isolated 13.42 g of (I) with b.p. 82.5-84.5° at 20 mm and n_D^{20} 1.5774.

Condensation of 1-(α -furyl)-3-methyl-1,3-butadiene (I) with maleic anhydride. Experiment A. We placed 13.1 g of maleic anhydride, 17.9 g of (I), and 67 ml of absolute ether in a conical flask. When the substances were mixed, a canary yellow color appeared and after solution of the maleic anhydride there was a marked rise in the temperature of the mixture. It was cooled to room temperature with water. After an hour, separation of crystals of the monoadduct began. After the reaction had proceeded for four days at 18-20° the crystals were separated, washed with ether, and dried over sulfuric acid. We obtained 22.70 g (73.2%) of transparent tetrahedral prismatic crystals of monoadduct (IV) with m.p. 73.5-74.5°. The fractions of crystals (3.01 and 0.55 g) isolated by fractional crystallization of 5.0 g of monoadduct from a mixture of benzene and benzine melted at the same temperature.

Found %: C 67.16; H 5.22. $C_{17}H_{14}O_4$. Calculated %: C 67.23; H 5.21.

Hydrolysis of 5.9 g of monoadduct with water (100 ml) when the mixture was heated on a water bath gave 4.67 g (73.5%) of light yellow crystals of a dibasic acid (VI) with m.p. 164-165°. Fractional crystallization of 3.60 g of the acid from a mixture of ethyl acetate and benzine gave fractions of crystals (1.55 and 0.90 g) with m.p. 166-167°.

Found %: C 62.37; H 5.69. $C_{17}H_{14}O_5$. Calculated %: C 62.39; H 5.65.

Experiment B. We placed in a flask 4.90 g of maleic anhydride, 3.35 g of (I), and 25 ml of absolute ether. After a day at room temperature crystals of the bisadduct began to separate. After the reaction had taken place for five months the mixture crystallized. The crystals of bisadduct were filtered off in an atmosphere of nitrogen, washed with absolute ether, and dried over sulfuric acid. We obtained 6.87 g (83.30%) of crystalline bisadduct (V) in the form of light yellow grains. The melting point was not constant and changed considerably (101.0-102.0°; 105.0-105.5°) with slight changes in rate of heating.

Found %: C 61.59; H 4.45. $C_{17}H_{14}O_7$. Calculated %: C 61.82; H 4.27.

Condensation of the monoadduct with maleic anhydride. We placed in a flask 11.6 g of monoadduct (IV), 4.9 g of maleic anhydride, and 12.0 ml of acetone. After standing for a day at 18-20° white granular bisadduct began to separate and after four days the reaction mixture was full of it through almost the entire volume. We separated 6.80 g (41.20%) of crystalline bisadduct (V) with the above properties.

Found %: C 61.91; H 4.48. $C_{17}H_{14}O_7$. Calculated %: C 61.82; H 4.27.

SUMMARY

1. We have defined the conditions for dehydration of 1-(α -furyl)-3-methyl-1-buten-3-ol to 1-(α -furyl)-3-methyl-1,3-butadiene in the presence of iodine.
2. We have shown that 1-(α -furyl)-3-methyl-1,3-butadiene with maleic anhydride in the ratio 1 : 1 first reacts with the conjugated system of double bonds of the side chain with formation of the monoadduct, the anhydride of 3-(α -furyl)-5-methyl-1,2,3,6-tetrahydrophthalic acid. On hydrolysis it gives 3-(α -furyl)-5-methyl-1,2,3,6-tetrahydrophthalic acid.
3. Condensation of 1-(α -furyl)-3-methyl-1,3-butadiene with maleic anhydride in the molar ratio 1 : 2 and also condensation of the monoadduct with maleic anhydride give a bisadduct.

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THE SYNTHESIS OF ASYMMETRIC ION EXCHANGE RESINS BASED ON L-TYROSINE

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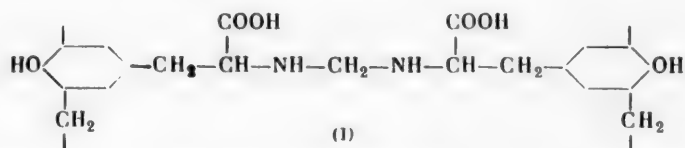
Recently the question of separation of racemates on asymmetric adsorbents has attracted more attention. There have been a number of reviews of this problem [1, 2]. The interest in the asymmetric adsorbents is explained by the fact that such adsorbents are potential reagents for separating racemates and that asymmetric adsorbents can be used for establishing the configuration of substances and for identification of natural amino acids [2, 3]. The natural adsorbents (starch, lactose, etc.) are beginning to be replaced by specially synthesized ones [2, 3].

This theoretical and practical interest raises the question of the possibility of separating racemates on asymmetric ion exchange resins. Such a resin was prepared by Grubhofer and Schleith who used a commercial symmetrical carboxy-containing resin "Amberlite XE-64," esterifying it with quinine on its secondary hydroxyls [4, 5]. Bunnnett and Marks synthesized an asymmetric resin of the phenol-formaldehyde type by condensing N-(p-hydroxyphenyl)-butyric acid with formaldehyde in the first case and with p-toluenesulfonyl-L-tyrosine in the second [6]. The resin obtained by Grubhofer and Schleith was not sufficiently suitable for studying ion exchange because of the low stability of the ester bond, as the authors themselves noted. The resins obtained by Bunnnett and Marks were stable enough. However, as these authors showed, separation of racemates on these resins did not take place. One of the possible reasons for this was considered by the authors to be reaction of the separated substances with the resin at only one point, since only carboxyl reacts with the bases.

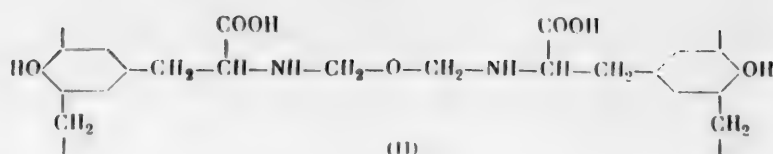
We have attempted to synthesize ion exchange resins based on unsubstituted L-tyrosine. Such a choice is warranted by the stability of optically active tyrosine in respect to racemization and the presence in tyrosine of three active groups (OH, COOH, and H₂N) with the carboxyl and amino groups close to the center of asymmetry which increases the probability of different reactions of the optical antipodes with tyrosine. There is increased probability of separation in view of the greater "concentration" in the resin of optically active substances than in the case of Bunnnett and Marks. Finally, it is also important that the optically active isomer of tyrosine is available commercially.

It is known that linear polymers as a rule are soluble. Since in tyrosine the para-position to the hydroxyl group is occupied, we have the right to expect that in the condensation of tyrosine with formaldehyde only linear polymers will be formed. Therefore in the first experiments we used phenol or phenoxyacetic acid as a cross agent. The condensation product of formaldehyde with phenoxyacetic acid and tyrosine was very interesting in its physical and chemical properties. We will call this resin TPF.

In the course of this work we showed that tyrosine can give with formaldehyde an insoluble polymer even without addition of cross agents.* Evidently in this case there is a joining of the linear polymers because of reaction of the formaldehyde with the amino groups of the tyrosine molecule. Here there is the possibility of formation between the nitrogen atoms of methylene (I) or ether bonds (II).



* There is evidence in the literature of the formation of high molecular substances when tyrosine is heated with formaldehyde [7].



It should be mentioned that there is a description in the literature of a case of formation of such bonds between the nitrogens in the polycondensation of amides [8]. The data of elementary analysis for nitrogen show that most probably there is a second type of condensation.

The resulting resins have a brownish-yellow or light yellow color, resembling KFU in mechanical properties [9]. The resins from alkaline condensation are more elastic, and at high temperature almost resinous. The resins are sufficiently stable in chemical respects. We have not noted any change in properties of the resins as a result of numerous conversions from the H⁺ form to the sodium form and back. The resins are insoluble in acids and alkali, dioxane, benzene, acetone, water, and other ordinary solvents; they luminesce with a greenish-yellow color when illuminated with a bactericidal lamp. Data on the swelling of the synthesized resins in water and alkali and the static volume capacity are given in Table 1.

TABLE 1

Resin*	Swelling coefficient		Full static capacity (in mg equiv./g)
	water	1 N KOH	
TFK-2	1.5	4.7	5.6
TFK-4	1.4	4.9	5.1
TFO-2	1.4	5.9	5.4
TFO-4	2.9	5.5	7.7
TFF.	1.2	4.2	3.5

* The data are given for the dry resins in the H⁺ form.

Since tyrosine contains an amino group besides the carboxyl and hydroxyl groups, we can assume that the synthesized resins will be amphoteric to some extent.

This assumption was verified as follows. The resin in the H⁺ form, obtained by washing to pH 4-5, after treatment with hydrochloric acid was treated for a day with 50 ml of 0.1 N KOH. After this chloride ions were absent

from the solution, and the acidified solution did not give a precipitate with silver nitrate. Elementary analysis of the resin in the hydrogen form showed the definite absence of chloride ion. In order to demonstrate the anion exchange properties of the resin, we treated the hydrogen form of the resin with 0.1 N solution of acid and after a day determined the change in acid concentration. From the change in concentration we calculated the capacity of the resin for chloride ions. The results are given in Table 2.

TABLE 2. Full Static Capacity with Chloride Ion

Resin	Capacity (in mg-equiv./g)
TFK-2	1.35
TFK-4	1.50
TFO-2	1.31
TFO-4	1.33
TFF.	0.55

On the basis of these results we can assert that the resin is amphoteric, and the anion exchange properties of the resin are shown weakly.

During the synthesis of the high polymers, racemization of the tyrosine is evidently absent. According to the literature, tyrosine is racemized with difficulty. Thus, according to [10] for full racemization of tyrosine it is necessary to heat it for five hours with baryta water at 170°. According to [11] tyrosine is racemized by boiling for many days with alkali. Tyrosine is not changed by heating to 240° with hydrochloric acid saturated at 0° [12]. Thus, the

conditions for racemization of tyrosine are considerably more severe than those under which the synthesis is carried out. It is also apparent that we obtain an asymmetric resin, since the aqueous extract from the synthesized resins was optically active. The specific rotation of the solid substance obtained by evaporation of the water extract was -30 to -35° , while the specific rotation of tyrosine is -8° .

EXPERIMENTAL

Synthesis of resin TFK-4. In a three necked flask with a stirrer, thermometer, and reflux condenser were introduced successively 10.4 ml of 33% HCl and 8.8 ml of 40% formaldehyde. With heating on a bath to 60° and rapid stirring tyrosine was added to the vessel. After full solution of the tyrosine, the mixture was kept for 40 minutes at $90-95^\circ$ and then 1.2 ml of 50% sulfuric acid and 4 g of paraform were quickly added and the mixture was stirred until a homogeneous mass was obtained. Then the mixture was kept for 1.5 hours in an air thermostat at 100° and for 1 hour at $120-125^\circ$. The resulting porous, rather friable product had a brownish-yellow color.

Found %: C 62.9; H 5.73; O 25.7; N 5.63.

Synthesis of resin TFK-2. This was carried out in the same way, except that the time of keeping on the bath before adding the paraform and sulfuric acid was 30 minutes, then 45 minutes on the water bath at 90° and 2.5 hours in the drying cabinet at 120° .

Synthesis of resin TFF. Twenty g of tyrosine and 20 g of phenoxyacetic acid were dissolved in a mixture of 17.6 g of 40% formaldehyde and 10.4 ml of 33% hydrochloric acid with rapid stirring at $60-70^\circ$. After solution and one hour boiling on a water bath we added 1.2 ml of sulfuric acid and 4 g of paraform. The resin was kept for 1.5 hours at $90-95^\circ$ on a water bath and then was transferred to the drying cabinet where it was kept for 1.5 hours at 120° .

Synthesis of resin TFO-2. Twenty-five g of tyrosine was dissolved with heating and rapid stirring in 37.5 ml of formaldehyde and 12.5 ml of 40% sodium hydroxide. The tyrosine was added in portions. Solution occurred with heating. The last portions dissolved with difficulty. The mixture was placed on a water bath at 90° , where after several minutes it changed into a very thick, porous mass, and was kept for 1.5 hours on the water bath, then ground to a size of 0.5 cm in diameter and placed in an open porcelain crucible in a thermostat where it was kept for 4.5 hours at $120-125^\circ$. Yield of TFO-2 and the other resins was close to 100%.

Found %: C 61.4; H 6.2; O 27.0; N 5.5.

Synthesis of resin TFO-4. This was synthesized in the same way as in the previous case, but was kept on the water bath for two hours and in the drying cabinet at $100-110^\circ$ for 100 minutes.

Determination of full static volume capacity. The capacity was determined in the usual way [13]. We added 50 ml of 0.1 N KOH to 0.5 g of resin and after 24 hours determined the concentration of alkali in the filtrate, from which we calculated the capacity. The resin used was air dried; the data on capacity, shown in Table 1, are calculated on the dry resin.

The swelling coefficient was determined as follows: 1 ml of air dried resin was placed in a measuring cylinder and 9 ml of water or 1 N KOH were added. The cylinder stood for a day in a horizontal position. Then the cylinder was placed vertically and the volume was determined. From this we calculated the swelling coefficient.

Determination of the specific rotation was carried out as follows: a sample of freshly synthesized resin TFO-4 (about 1 g) was placed in a test tube with 15 ml of water. The solution acquired a yellow color. We determined the rotation of the solution on a circular CM polarimeter. It was -0.08° (average of three experiments), and each time we calculated the average of ten measurements. Then the solution was evaporated dry and the amount of substance determined by weighing. From this we calculated the specific rotation, $[\alpha]_D^{20} -30^\circ$.

SUMMARY

1. By direct polycondensation of L-tyrosine with formaldehyde (in the presence of alkali and also acid catalysts) and L-tyrosine with phenoxyacetic acid and formaldehyde we have obtained insoluble polymers which contain an asymmetric carbon atom.
2. We have shown that these polymers have cation exchange properties. Anion exchange properties are shown weakly.
3. We have determined the full static capacity and swelling coefficient for the synthesized cationites.

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AZOMETHINE DYES WHICH CONTAIN A PHOSPHONIC GROUP*

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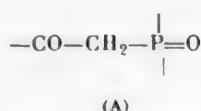
Azomethine dyes are derivatives of various ketomethylene compounds with residues of substituted *p*-diamines and have recently become of great practical significance, since they are substances which are used in color cinematography [1].



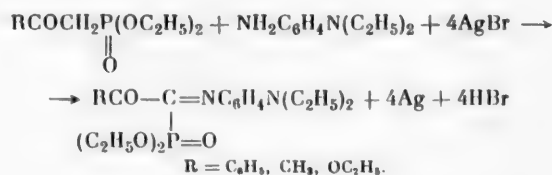
It is known from the literature [2-4] that for the formation of yellow azomethine dyes, compounds are usually used which contain active methylene groups in an open chain connected with two carbonyl groups. Such compounds are β -diketones and different derivatives of acyl acetic acids, of which the most important is the substituted anilide of benzoylacetic acid.

As A. E. Arbuzov showed [5] there is a deep analogy between carboxyl and phosphonic groups. The phosphorus analog of acetoacetic ester, acetone phosphoric acid ester, and benzoylacetic ester, acetophenone phosphonic ester, react with metallic sodium [6, 7]. Kosolapoff [8] showed that methane diphosphonic acid can also replace hydrogen of the methylene group by a metal. Other properties of β -ketophosphonic acid derivatives also confirm their similarity with β -ketocarboxylic acid [9, 10].

Therefore we predicted the formation of yellow azomethine dyes for derivatives of β -ketophosphonic acids which contained active methylene groups in the open chain connected with carbonyl and phosphonic groups (A).



Our prediction was fulfilled. On development of an exposed silver bromide emulsion by *p*-diethylaminoaniline in the presence of diethyl acetonephosphonate, diethyl acetophenonephosphonate, or triethyl phosphonoacetate, the corresponding azomethine dyes which contained the phosphonic group were formed.



* Read at the II Congress on Chemistry and Use of Phosphoorganic Compounds, November 30, 1959 (Kazan).

As color photographic studies showed, diethyl acetophenonephosphonate, diethyl acetonephosphonate and triethyl phosphonoacetate under conditions of color development from yellow azomethine dyes with the color developer and in activity of azomethine dye formation did not yield at all to the analogous esters of the corresponding aceto-, benzoylacetic and malonic acids.

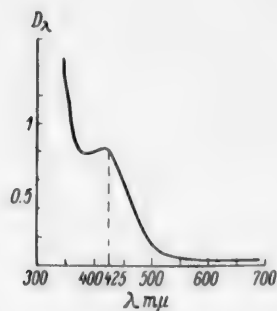


Fig. 1. Curve of spectral absorption of the dye from diethyl acetophenonephosphonate, formed under conditions of color development.

times more colored zones. Usually the upper zone consisted of tarry products, the middle zone of an orange dye of unknown structure, and the lower was the yellow azomethine dye which was desorbed from the aluminum oxide by chloroform. To obtain the pure azomethine dye we submitted the latter to two to three chromatograms, and purified by extraction and recrystallization.

In Fig. 2 we give the curves of spectral absorption of the dyes in ethyl alcohol; and in the table, the dyes which were synthesized.

As the results in the table show, when potassium ferricyanide is used as the oxidizing agent, the yield of dye is small; therefore "method a" is not of practical value. The synthesized dyes were orange, crystalline substances, easily soluble in ether, chloroform, acetone, dioxane, and benzene, difficultly soluble in alcohol, practically insoluble in water. The yellow color of these dyes, on acidification, passed into red as a result of salt formation with formation of a cation which probably has a quinoid structure.

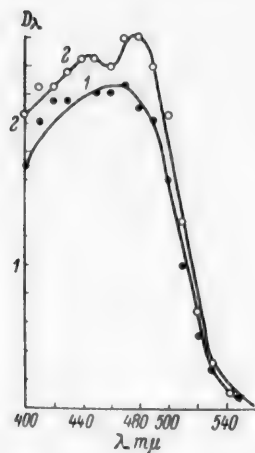


Fig. 2. Curve of spectral absorption of the dyes in ethanol. 1) Dye from diethyl acetophenone phosphonate; 2) dye from diethyl acetonephosphonate.

One of the chief requirements for the yellow components is that they be sufficiently reactive under the conditions of color development. Dyes formed from these components should have selective absorption with maximum spectral absorption at 430-440 mμ. The results of color photographic study showed that of the above three components diethyl acetophenonephosphonate is the most reactive in color development in the sense of the formation from it of dye under the conditions of color development as compared with the other two; the dye from it has the best selective absorption with a spectral maximum absorption at 425-430 mμ (Fig. 1).

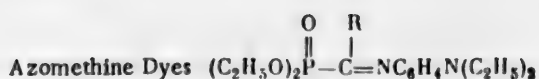
The azomethine dyes from diethyl acetonephosphonate and diethyl acetophenonephosphonate with diethyl p-phenylenediamine were synthesized with the use of potassium ferricyanide (method a) or silver chloride (method b) as the oxidizing agent. Formation of the azomethine dye was then usually accompanied by side processes; the pure substance could be isolated only by use of chromatography on aluminum oxide of their chloroform solutions. In all cases on chromatography of the dyes there was observed formation of two and some-

A characteristic of the azomethine group of azomethine dyes without a phosphonic group is the ease of their splitting in water solution, especially when heated or acidified [11]. Such instability makes them little fit for use. As we showed in our experiments on the stability of the azomethine group in azomethine dyes which contain the phosphonic group, the introduction of the phosphonic group instead of the carbonyl greatly raises the stability of the azomethine group. It is not decomposed by long heating with water and is stable to acids and alkalis.

EXPERIMENTAL

The starting substances were synthesized by the Arbuzov reaction [12] by reaction of triethylphosphite with monobromoacetic ester, bromoacetone, and bromoacetophenone. This we obtained respectively: triethyl phosphonoacetate, b.p. 142-143° (12 mm), n_D^{20} 1.4315 [14], diethyl acetone phosphonate, b.p. 132-135° (13 mm), n_D^{20} 1.4380, d_4^{20} 1.1253 [13, 15, 16], and diethyl acetophenonephosphonate, with b.p. 192-193° (11 mm), n_D^{20} 1.5140, d_4^{20} 1.1810 [13, 17].

Azomethine dye from diethyl acetonephosphonate (I). Synthesis of the dye with the oxidizing agent potassium ferricyanide (method a). In a 1 liter beaker with a mechanical stirrer we placed a solution of 1.61 g of diethyl acetonephosphonate in 220 ml of 95% alcohol. We added a solution of 4 g of anhydrous



R	Method of pre- paration	M. p.	Absorption maximum in ethanol mμ	Yield, %	% P	
					calcu- lated	found
(I) CH ₃ CO {	a b	149–152° 149–152	470–480	2–3.5 18–21.2	8.74	8.95
(II) C ₆ H ₅ CO {	a b	156–158 156–158	470	2.0 55.3		
					7.44	7.70

soda in 50 ml of water and then a solution of 2.89 g of diethyl p-phenylenediamine sulfate in 50 ml of water. To the stirred mixture we added a solution of 13.17 g of potassium ferricyanide in 100 ml of water. After 15 minute stirring, the dye was extracted with ether. The extract was washed with water to full removal of the colored substance in the water, chromatographed on aluminum oxide, and washed off with chloroform. After three chromatographic separations with later extractions of the mixture with water we obtained 0.1252 g of pure dye (table).

Synthesis of the dye using silver chloride as the oxidant (method b). To a solution of 2.32 g of sodium chloride in 28 ml of water we slowly added a solution of 6.12 g of silver nitrate in 28 ml of water and to the resulting suspension of silver chloride we added successively the solutions: 8.59 g Na₂CO₃ · 10H₂O in 16 ml of water, 0.776 g of diethyl acetonephosphonate in 20 ml of methyl alcohol, and 1.16 g of diethyl p-phenylenediamine sulfate in 32 ml of water. After 30 minute stirring at room temperature the precipitate was filtered off, washed with water to disappearance of alkali, and dried. The dye was extracted from the filter with chloroform, chromatographed on aluminum oxide, and removed with chloroform. After three chromatographic treatments with later extraction by water we obtained 0.025 g of azomethine dye (table).

Azomethine dye from diethyl acetophenonephosphonate (II). Synthesis of the dye by method a. The method of preparing and purifying the dye was completely analogous to the previous experiment. In the reaction we took 1.5 g of diethyl acetophenonephosphonate in 120 ml of 95% alcohol, 3 g of anhydrous soda, in 30 ml of water, 1.73 g of diethyl p-phenylenediamine sulfate in 30 ml of water, and 7.9 g of potassium ferricyanide. We obtained 0.0318 g of azomethine dye (table).

Synthesis of the dye by method b. The method of preparing and purifying the dye was completely analogous to method b of the previous experiment. In the reaction we took 3.06 g of silver nitrate in 14 ml of water, 1.16 g of sodium chloride in 14 ml of water, 1.6 g of soda in 8 ml of water, 0.51 g of diethyl acetophenonephosphonate in 10 ml of methyl alcohol, and 0.58 g of diethyl p-phenylenediamine sulfate in 16 ml of water. We obtained 0.04 g of dye. Besides this we obtained 0.005 g of orange dye of unknown structure, easily soluble in chloroform, ether, and acetone, insoluble in water. On acidification of the solution of the latter dye with dilute hydrochloric acid there was change of red color into violet, and on following addition of alkali, into the original red.

Study of the Stability of the Dye from Diethyl Acetonephosphonate to Alkali and Acid

1. Acidification of the yellow dye with a great excess of concentrated hydrochloric acid gave a water solution of a red dye which was boiled in a flask with a reflux condenser for five hours. During three hours no decomposition was found. Decomposition began only on five hour boiling.

2. A saturated dioxane solution of the dye was heated with excess ammonia for five hours at 100°. There was no decomposition of the dye. At the end of this time the solution was acidified with dilute hydrochloric acid to the appearance of a red color, and heated for 13 hours more at 100°. Under these conditions decomposition of the dye was absent: when the solution was made alkaline, the red color turned to yellow, and on acidification, to red.

Thus, this dye is very stable to the action of relatively high temperature (100°) and weak alkali or acid water solutions.

SUMMARY

1. We have shown the possibility of formation of azomethine dyes by reaction of aromatic diamines with phosphoorganic compounds which contain an active methylene group bound to a carbonyl and a phosphonic group.
2. We have synthesized the first two examples of this new class of azomethine dyes which contain the phosphonic group and studied their absorption spectra in ethanol.
3. We have found that these dyes are favorably distinguished by their stability to acids, alkalis, and high temperature as compared to other azomethine dyes.
4. The results of color photographic study show that diethyl acetophenonephosphonate is the most reactive in the sense of the formation from it of an azomethine dye under the conditions of color development. The dye from it has good selective absorption with an absorption maximum at 425-430 m μ .

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THE SYNTHESIS OF SOME MIXED TRIALKYL THIOPHOSPHATES AND ALKYLARYL PHOSPHITES

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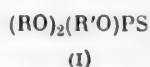
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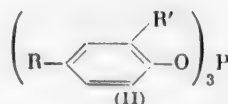
Original article submitted October 10, 1960

Some phosphoorganic compounds have found wide use as additives for various petroleum fractions. Full esters of phosphorous acid, the trialkyl (aryl) phosphites, and some of their derivatives are used as antioxidizing additives for mineral oils [1-4].

For study of the antioxidizing properties with respect to oil products and the antioxidizing activity with respect to the structure of organic phosphorous compounds we have carried out the synthesis of compounds with the general formulas (I) and (II)



R and R' are different
aliphatic radicals



a) R = *tert*-C₅H₁₁, R' = H
b) R = R' = *tert*-C₅H₁₁

The synthesis of compounds of type (I) was carried out by adding elementary sulfur to the corresponding mixed trialkyl phosphite



In their turn, the mixed trialkyl phosphites were synthesized by the reaction of partial transesterification [5-7]. The syntheses of tri(4-*tert*-amyl)- and tri(2,4-di-*tert*-amyl)-phenylphosphite (II) were carried out by reaction of the corresponding 4-*tert*-amyl- and 2,4-di-*tert*-amylphenols [8] with phosphorus trichloride.

TABLE 1. Addition of Sulfur to Phosphites

Product obtained	Taken for reaction, g		Bath temperature	Duration of heating, hrs	Yield, %
	Trialkyl phosphite	Sulfur			
PS(OC ₂ H ₅) ₂ (OC ₄ H ₉ -n.) ₂	5.21	0.74	80-100°	4	88.4
PS(OC ₂ H ₅) ₂ (OC ₃ H ₇ -n.) ₂	3.10	0.55	120-150	5	94.1
PS(OC ₂ H ₅) ₂ (OC ₅ H ₁₁ -iso) ₂ *	3.05	0.42	80-100	2	66.7
PS(OC ₂ H ₅) ₂ (OC ₅ H ₁₁ -iso) ₂ *	4.00	0.52	120-140	5	51.1
PS(OC ₂ H ₅) ₂ (OC ₃ H ₇ -n.) ₂ *	0.92	0.155	110-115	3	70.9
PS(OCH ₃) ₂ (OC ₃ H ₇ -n.) ₂	0.76	0.16	80-90	7	91.3
PS(OCH ₃) ₂ (OC ₃ H ₇ -n.) ₂	0.90	0.16	80-100	6.5	82.1
PS(OC ₃ H ₇ -n.) ₂ (OC ₄ H ₉ -n.) ₂	0.47	0.063	80-90	7	80.85
PS(OCH ₃) ₂ (OC ₂ H ₅) ₂ (OC ₃ H ₇ -n.)	0.64	0.123	80-90	7	84.2
(4-C ₅ H ₁₁ -C ₆ H ₄ O) ₃ PS	2.50	0.16	150-200	11	84.9

TABLE 2. Physical Constants and Analyses of the Synthesized Trialkyl Thiophosphates (RO)₃(R'O)PS

No.	Formula	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR _D		Empirical formula		% P	
					Found	Calc.			Found	Calc.
1	P(S)(OC ₂ H ₅) ₂ (OC ₄ H ₉ -n) ₂	129-130° (14)	1.4506	1.0041	68.12	68.19	C ₁₀ H ₂₃ O ₃ PS	12.35, 12.36	12.19	
2	P(S)(OC ₃ H ₇ -n) ₂ (OC ₂ H ₅) ₂	95-97° (13)	1.4507	1.0544	54.17	54.33	C ₇ H ₁₇ O ₃ PS	14.86, 14.91	14.64	
3	P(S)(OC ₃ H ₇ -n) ₂ (OC ₂ H ₅) ₂	Not determined	1.4405	1.0027	63.22	63.56	C ₉ H ₂₁ O ₃ PS	13.04	12.89	
4	P(S)(OC ₂ H ₅) ₂ (OC ₃ H ₇ -iso) ₂	135-148° (12)	1.4510	0.9856	77.16	77.42	C ₉ H ₂₁ O ₃ PS	11.46	10.97	
5	P(S)(OC ₂ H ₅) ₂ (OC ₃ H ₇ -iso) ₂	226-227°	1.4505	1.0443	58.30	58.95	C ₈ H ₁₉ O ₃ PS	13.82	13.69	
6	P(S)(OC ₃ H ₇ -n) ₂ (OC ₂ H ₅) ₂	213-214°	1.4530	1.0103	45.06	45.09	C ₇ H ₁₃ O ₃ PS	16.46, 16.50	16.80	
7	P(S)(OC ₂ H ₅) ₂ (OC ₃ H ₇ -n) ₂	216-217°	1.4520	1.0618	53.95	54.33	C ₇ H ₁₃ O ₃ PS	14.91, 14.81	14.60	
8	P(S)(OC ₂ H ₅) ₂ (OC ₃ H ₇ -n) ₂	259-260°	1.4460	0.9837	72.76	72.80	C ₁₁ H ₂₃ O ₃ PS	11.80	11.55	
9	P(S)(OC ₂ H ₅) ₂ (OC ₃ H ₇ -n) ₂	208-209°	1.4510	1.0925	48.87	49.71	C ₈ H ₁₅ O ₃ PS	15.40, 15.42	15.60	
10	(4-C ₅ H ₁₁ -C ₆ H ₄ O) ₃ P(S) **		1.5485	1.0768	163.10	163.59	C ₃₃ H ₄₅ O ₃ PS	5.61	5.60	

* B.p. determined by the method of Linstead [9].

** Solidified on keeping.

The addition of elementary sulfur to tri(4-tert-amyl)-phenyl phosphite gave the corresponding thio derivative (Table 2).

EXPERIMENTAL*

Synthesis of tri(4-tert-amyl)phenyl phosphite. In a three necked flask fitted with a reflux condenser and thermometer was placed 19.49 g of p-tert-amylphenol. After the latter had melted we added in small portions 6.4 g of phosphorus trichloride. The contents of the flask were heated at 230-240° with shaking for two hours, and then for another four hours at 250-255° and dried carbon dioxide gas was passed in. The residue of easily volatile products and phenol were distilled off in a vacuum. We thus obtained a viscous liquid. The product was decolorized by heating with activated charcoal at 280° for one hour.

We obtained 19.46 g (93.4%) of a light yellow liquid.

B.p. 284°, n_D^{20} 1.5420, d_4^{20} 1.0457, MR_D 156.7; calc. 156.86.

Found %: P 6.20, 6.30. C₃₃H₄₅O₃P. Calculated %: P 5.95.

Synthesis of tri(2,4-ditert-amyl)-phenyl phosphite. In a three necked flask fitted with a reflux condenser and thermometer we placed 25.16 g of 2,4-ditert-amylphenol. We added in small portions 5.5 g of phosphorus trichloride in 30 minutes with mixing at 40-50°. Then the reaction mass was heated for three hours with shaking at 230-245° and for another two hours at 280-290° while passing dried carbon dioxide gas. After distillation in a vacuum (15 mm, bath temperature 280-300°) we obtained 4.9 g of 2,4-ditert-amylphenol which had not reacted; we obtained 20.8 g (98%) of tri-(2,4-ditert-amyl)-phenyl phosphite.

n_D^{20} 1.5238, d_4^{20} 0.9861, MR_D 226.82; calc. 226.13.

Found %: P 4.53, 4.48. C₂₈H₃₈O₃P. Calculated %: P 4.23.

Tri(2,4-ditert-amyl)-phenyl phosphite was a light yellow, very viscous liquid which solidified on keeping.

Synthesis of mixed trialkyl thiophosphates. The reaction of addition of sulfur to the mixed trialkyl phosphites was carried out in a flask with a reflux condenser at first at room temperature and then for completion of the reaction the mixture was heated for a definite time. The small excess of sulfur was filtered off, n_D^{20} and d_4^{20} were determined, the b.p. was taken and analysis for P was run.

The conditions for carrying out the reaction are given in Table 1.

* Students V. R. Khalikov and A. A. Syrova took part in the experiments.

The mixed trialkyl thiophosphates could not be purified by distillation, since they were easily disproportionated when they were heated.

The mixed trialkyl thiophosphates were mobile liquids; most of them did not have an odor; they were insoluble in water and easily soluble in petroleum products and organic solvents.

In Table 2 we give the physical constants and results of phosphorus analysis for the compounds which we synthesized.*

SUMMARY

We have synthesized and identified twelve new compounds, not described in the literature; tri(4-tert-amyl)-phenyl phosphite and tri(2,4-di-tert-amyl)-phenyl phosphite and ten trialkyl thiophosphates.

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* The low yield of products is explained by the fact that the products were submitted to vacuum distillation (see Table 2).

PREPARATION OF ETHYL ESTERS OF β -METHYLENE- β -ACYLPROPIONIC ACIDS AND RELATED COMPOUNDS

V. B. Piskov

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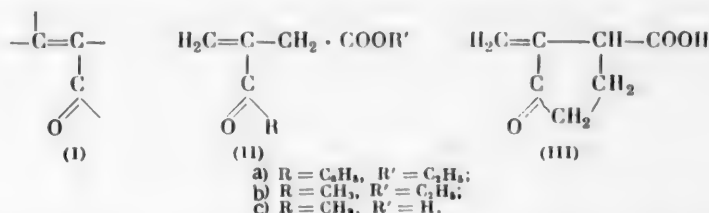
pp. 2937-2941, September, 1961

Original article submitted March 7, 1960

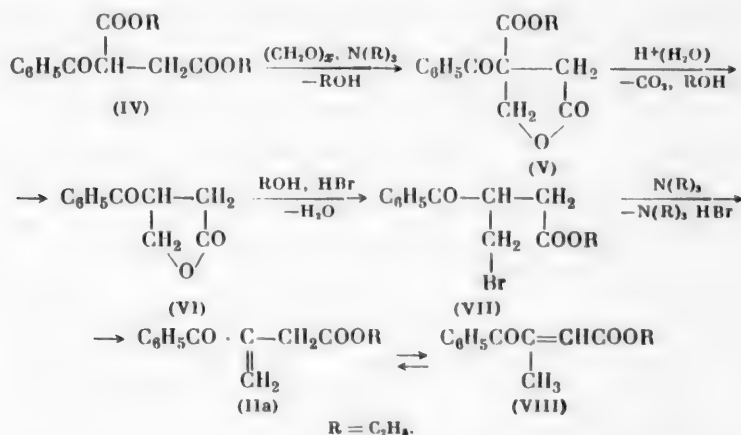
Well-marked antitlastic activity is exhibited by α , β -unsaturated aldehydes (in particular citral), α , β -unsaturated ketones, furfurylideneacetone and related compounds, sarcomycin and its analogs, a series of steroid hormones), and γ - δ - lactones of some unsaturated hydroxyacids (e.g., parasorbic acid and patulin) [1-7].

All these compounds contain a double bond conjugated with a carbonyl group. The biological activity in question is associated in our opinion with the presence of this grouping (I). This fact may serve as a lead in the search for new and more active preparations both among known substances and among substances to be synthesized in the future.

In continuation of our work in this direction [8], we have synthesized a series of compounds of the type of (II) which contain the grouping (I) and possess structural features also present in sarcomycin (III).



The ethyl ester of β -methylene- β -benzoylpropionic acid (IIa) was synthesized by our earlier method [8], starting from diethyl benzoylsuccinate (IV):

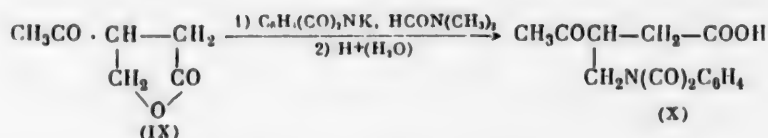


The resulting ester (IIa) gives the hydroxamic reaction, forms a 2,4-dinitrophenylhydrazone, and decolorizes bromine in CCl_4 . Separation of formaldehyde after ozonolysis of ester (IIa) confirms the presence of a methylene double bond. The low yield of dimedon derivative of formaldehyde (15%) and the unsharp melting point of the hydrazone of ester (IIa) can be explained by the existence of an equilibrium between ester (IIa) and its structural isomer (VIII) (cf. [9]).

The ethyl ester of β -methylene- β -acetylpropionic acid (IIb) was prepared from β -acetyl- γ -butyrolactone (IX) [8] by means of transformations analogous with those previously reported for the benzoyllactone (VI). The structure of ester (IIb) was confirmed by its saponification with 2 N H_2SO_4 to β -methylene- β -acetylpropionic acid (IIc).

This acid (IIc) (m.p. 69°) titrates with 0.1 N NaOH as a monobasic acid, forms a calcium salt with $\text{Ca}(\text{OH})_2$, decolorizes bromine water, and gives a 2,4-dinitrophenylhydrazone with m.p. $210\text{--}211^\circ$ [10]. Formation of formaldehyde on ozonolysis of acid (IIc) confirms the presence of a methylenic double bond.

It should be noted that lactone (IX) reacts with facility with potassium phthalimide in dimethylformamide solution to form the nicely crystallized phthalimide derivative (X).



This method can probably also be utilized for characterization of other lactones (cf. [11]).

The biological activity of the prepared compounds is now being studied.

EXPERIMENTAL

β -Benzoyl- β -carbethoxy- γ -butyrolactone (V). A solution of 1 g of K_2CO_3 in 1 ml of water was added in two portions to a mixture of 123 g of the ester of ketoacid (IV), 75 g of 36% formalin, and 100 ml of alcohol at 20° . The temperature of the mixture rose by $3\text{--}4^\circ$. After it had been allowed to stand for four days at room temperature, the reaction mixture was acidified with 6 N H_2SO_4 , diluted with ethyl acetate, washed with water, and dried with sodium sulfate. The ethyl acetate was distilled in vacuo on a water bath, and the residue distilled to give lactone (V); yield 41 g (35%).

B.p. $153\text{--}156^\circ$ (0.5 mm), n_D^{22} 1.5320.

The 2,4-dinitrophenylhydrazone of lactone (V) melts at 184° (from a mixture of alcohol and benzene).

Found %: C 54.24; H 4.22; N 12.63. $\text{C}_{20}\text{H}_{18}\text{O}_8\text{N}_4$. Calculated %: C 54.30; H 4.10; N 12.67.

β -Benzoyl- γ -butyrolactone (VI). A mixture of 250 ml of concentrated HCl, 140 ml of water, 180 ml of acetic acid, and 24 g of lactone (V) was stirred at $66\text{--}68^\circ$ until it became homogeneous (about 2 hr); the stirrer was then stopped and the reaction mass kept for 78 hr at $66\text{--}68^\circ$. It was decolorized with carbon, filtered, and evaporated on a water bath in vacuo at $50\text{--}60^\circ$. To the oily residue was added 25 ml of a mixture of alcohol and ether. Lactone (VI) crystallized on standing in the cold; yield 9 g (52%); m.p. 65° (from 70% alcohol [12]), λ_{max} 246μ .

Found %: C 69.40; H 5.30. M (by titration) 189. $\text{C}_{11}\text{H}_{10}\text{O}_3$. Calculated %: C 69.47; H 5.30. M 190.2.

The 2,4-dinitrophenylhydrazone of lactone (VI) melts at 222° (from a mixture of alcohol and benzene).

Found %: C 55.17; H 3.92; N 15.04. $\text{C}_{17}\text{H}_{14}\text{O}_6\text{N}_4$. Calculated %: C 55.13; H 3.81; N 15.13.

Ethyl ester of β -bromomethyl- β -benzoylpropionic acid (VII). A mixture of 11.9 g of benzoyllactone (VI) and 70 ml of 50% alcoholic HBr solution was held for three days at 0° , then poured into ice-containing water (100 g), and extracted with benzene (three times with 10-15 ml). The benzene extracts were combined, washed with water (three portions of 10-15 ml each), and dried with sodium sulfate. The benzene was taken off in vacuo at $30\text{--}32^\circ$, and 17.9 g of unpurified bromoester (VII) was obtained in the form of a light-yellow oil; $n_D^{21.5}$ 1.5390.

Ethyl ester of β -methylene- β -benzoylpropionic acid (IIa). A solution of 10 g of ethyl ester of bromoacid (VII) in 10 ml of ether was treated with 20 ml of triethylamine. Triethylamine hydrobromide at once commenced to come down. The mixture was allowed to stand for three days at room temperature and then diluted with 100 ml of ether. After filtration, the liquid was evaporated in vacuo at 32° . To the residue (6.8 g) was added 120 ml of ether. The ethereal solution was washed twice with 8 ml of 8% hydrochloric acid and then three times with 10 ml of water. The mass was dried over sodium sulfate and evaporated in vacuo at $30\text{--}35^\circ$. The residual oil was distilled to give 5 g of ethyl ester of the ketoacid (IIa).

B. p. 104° (0.4 mm), d_4^{20} 1.1, n_D^{20} 1.5300, M_R 61.2; calc. 60.4.

Found %: C 71.52; H 6.67. $C_{13}H_{14}O_3$. Calculated %: C 71.54; H 6.47.

2,4-Dinitrophenylhydrazone of ester (IIa): m.p. 176-181° (from alcohol).

Found %: C 56.99; H 4.65; N 14.13. $C_{19}H_{18}O_6N_4$. Calculated %: C 57.28; H 4.55; N 14.07.

Ozonolysis of the ester of ketoacid (IIa). A solution of 0.44 g (2 mmole) of ester (IIa) in 25 ml of ethyl acetate, cooled to 0° in an ice bath, was ozonized for 15 min with 3.5% ozone at a speed of 20 mmole/hr.

After addition of 15 ml of water and 0.6 g of zinc dust, the solution was shaken for 30 min at 20°. The zinc dust was filtered off, the aqueous layer was separated, and the ethyl acetate layer washed with water (two lots of 10 ml each). The combined aqueous extracts were poured into a solution of 1 g of dimedon in 35 ml of alcohol. Crystallization commenced at once. The dimedon derivative of formaldehyde was separated and recrystallized from alcohol; m.p. 190°; yield 88 mg (15%).

Ethyl ester of β -methylene- β -acetylpropionic acid (IIb). To a solution of 94 g of dry HBr in 94 ml of alcohol at 0° was added 23.8 g of lactone (IX) in large portions with shaking. The reaction mass was held for three days at 0° and then poured into ice water (150 g). It was then extracted with ether (6 portions of 100 ml each), washed three times with water (15 ml each time), and dried with sodium sulfate. Evaporation of the ethereal solution in vacuo at 30° gave 42 g (95%) of unpurified ethyl ester of β -bromoethyl- β -acetylpropionic acid in the form of a light-yellow oil with n_D^{20} 1.4690. To an ice-cooled solution of 42 g of the bromoacid ester in 85 ml of ether was added 45 ml of triethylamine dropwise at such a speed that the temperature of the mixture did not rise above 20-25°.

After the whole of the triethylamine had been added, the reaction mass was allowed to stand overnight at room temperature, after which 150 ml of ether was added, and the triethylamine hydrobromide was filtered off. The ethereal solution was evaporated in vacuo at 30°. To the residue (28 g) was added 150 ml of ether. The ethereal solution was washed twice with 10 ml of water, dried with sodium sulfate, and evaporated in vacuo at 30°. The residual oil was distilled to give 25 g (91%) of ethyl ester of ketoacid (IIb).

B. p. 54° (1 mm), d_4^{20} 1.1031, n_D^{20} 1.4482, M_R 40.5; calc. 40.5.

2,4-Dinitrophenylhydrazone of ketoester (IIb): m.p. 119° (from alcohol).

Found %: N 16.44. $C_{14}H_{16}O_6N_4$. Calculated %: N 16.66.

β -Methylene- β -acetylpropionic acid (IIc). A mixture of 6.4 g of the ester of acid (IIb), 100 ml of 2 N H_2SO_4 , and 5 mg of hydroquinone was stirred for 40 hr at 32°C, the resulting solution was clarified with carbon, $NaHCO_3$ was added to give pH 8, and the mass was washed with 80 ml of ether. The aqueous solution was acidified with 2 N H_2SO_4 to pH 2, saturated with $(NH_4)_2SO_4$ (about 80 g), and extracted with ethyl acetate (5 times with 80 ml each). The ethyl acetate extracts were combined, clarified with carbon, and dried with Na_2SO_4 . The solvent was taken off in vacuo at 28°C. The residue crystallized after standing in the cold. Yield 4.2 g (80%) of acid (IIc), m.p. 69°C (from ether).

Found %: C 56.43; H 6.32. M (titration) 128. $C_6H_8O_3$. Calculated %: C 56.24; H 6.29. M 128.1.

2,4-Dinitrophenylhydrazone of acid (IIc): m.p. 210-211°C [10].

Found %: N 18.04. $C_{12}H_{12}O_6N_4$. Calculated %: N 18.18.

Ozonolysis of ketoacid (IIc). Through a solution of 0.3 g of ketoacid (IIc) in 15 ml of ethyl acetate at 0° was passed ozone at a speed of 20 mmole/hr for 6 min. To the solution was then added 15 ml of water and 500 mg of zinc dust. The mixture was boiled for 30 min on a water bath and was then filtered, without cooling, into a solution of 450 mg of dimedon in 15 ml of alcohol. Addition of 30 ml of water was immediately followed by commencement of crystallization. The precipitate was filtered, and washed with alcohol and ether. Yield 0.24 g (36%) of dimedon derivative of formaldehyde with m.p. 190° (from alcohol).

Phthalimide derivative of β -acetyl- γ -butyrolactone (X). To a solution of 4.9 g of lactone (IX) in 20 ml of $HCON(CH_3)_2$ was added 7.4 g of potassium phthalimide and the mixture stirred for 2 hr at 60°. The solution was cooled and 70 ml of ether was added. The resulting yellow oil was separated, washed with ether (twice with 80 ml each), dissolved in 10 ml of water, and strongly acidified with concentrated HCl. The precipitate was collected, washed with 10 ml of water and recrystallized from 50% aqueous alcohol. Yield 9 g (85%) of phthalimide derivative (XI) with m.p. 144°.

Found %: C 61.01; H 4.86. Neut. Equiv. 136.5. $C_{14}H_{15}O_5N$. Calculated %: C 61.09; H 4.76. Neutr. equiv. 137.5.

SUMMARY

The preparation of esters and derivatives of β -methylene- β -acylpropionic acids was described.

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ALKYLATION OF ARENESULFAMIDES BY 2-BUTANOL

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In a paper by one of us [1] it was shown that arenesulfamides are easily alkylated by 2-propanol and by cyclohexanol in 80-85% sulfuric acid at 60-70°; it was also established that under these conditions alkylation does not take place in the ring and that exclusively N-monoalkyl derivatives of the arenesulfamides are obtained in accordance with the stoichiometric equation



Disubstituted derivatives (I) are not obtained even with a considerable excess of the alcohol. Subsequently the alkylation reaction that we had discovered was extended to alkanesulfamides (II) and it was found that also in this case monoalkylated derivatives are obtained in good yield even with a lower concentration of sulfuric acid [2].



The purpose of the present work was the study of the alkylation of arenesulfamides by 2-butanol. Experiments showed that under similar conditions (80-85% sulfuric acid, 70°) only mono-sec. butyl derivatives of arenesulfamides are again obtained but with a slightly lower yield than is obtained in alkylation with 2-propanol or cyclohexanol. The resulting N-sec. butylarenesulfamides (II) usually give poorly soluble salts with caustic alkalies; they are easily extracted from aqueous solutions of alkalies with dichloroethane, which is used for purification from unreacted arenesulfamide. Arenesulfonyl sec.-butylamides are extracted from solution in 80% sulfuric acid by dichloroethane whereas unsubstituted arenesulfamides are not extracted. p-Aminobenzenesulfamide (sulfanilamide) is also alkylated under these conditions, but only at the sulfamido group, and p-aminobenzenesulfonyl sec-butylamide (III) is obtained, i.e., the aromatic amino group is not attacked under these conditions.

EXPERIMENTAL

Benzenesulfonyl sec.-butylamide (II, Ar = C₆H₅). To a solution of 15.7 g (0.1 mole) of benzenesulfamide 100 ml of 80% sulfuric acid heated to 70° was added 0.2 mole (100% excess) of 2-butanol in the course of 40 min, and the mixture was stirred for 5 hr at 70°. The warm mass was extracted with 100 ml of dichloroethane; the extract was washed with water, then with 100 ml of 1.5 N sodium hydroxide solution, and the dichloroethane was distilled with steam. A first extraction gave 9.9 g (46.4%) of solid product. Purification was effected by dissolution of the whole precipitate in a mixture of 10 ml of 40% sodium hydroxide and 50 ml of water and filtration of the hot solution on a glass filter; the precipitated sodium salt was isolated from the cooled solution by filtration; the still moist salt was dissolved in water with addition of sodium hydroxide, and ammonium chloride solution was added to bring down the product. Yield 8.15 g (38%) with m.p. 52-56°. Crystallization from aqueous methanol gave long, colorless needles with m.p. 65°; literature [3]: m.p. 70.5°.

p-Chlorobenzenesulfonyl sec.-butylamide (II, Ar = p-ClC₆H₄). was similarly prepared by alkylation of p-chlorobenzenesulfamide. Yield of uncrystallized product 59%, m.p. 64°. Purification via the sodium salt as above gave a product with m.p. 74°, yield 57%. Crystallization from methanol gave needles with m.p. 75-75.5°.

Found %: N 5.83. C₁₀H₁₄O₂NSCl. Calculated %: N 5.66.

3,4-Dichlorobenzenesulfonyl sec.-butylamide (II, Ar = 3,4-Cl₂C₆H₃) was prepared from 3,4-dichlorobenzenesulfamide by the preceding method but with double the volume of 80% sulfuric acid due to the poor solubility of 3,4-dichlorobenzenesulfamide. Recrystallization from n-heptane gave prismatic crystals with m.p. 78-80°.

Found %: N 5.14. C₁₀H₁₃O₂NSCl₂. Calculated %: N 4.96.

2,5-Dichlorobenzenesulfonyl sec.-butylamide (II, Ar = 2,5-Cl₂C₆H₃) was similarly prepared with a doubled volume of acid. Crystallization from alcohol gave scales with m.p. 125°; yield 48%.

Found %: N 5.00. C₁₀H₁₃O₂NSCl₂. Calculated %: N 4.96.

p-Ethylbenzenesulfonyl sec.-butylamide (II, Ar = p-C₂H₅C₆H₄) was prepared from p-ethylbenzenesulfamide by the same procedure as for benzenesulfonyl sec.-butylamide. The residue after steam-distillation of the dichloroethane was a dark oil with $n_D^{24.2}$ 1.5269, soluble in 10% sodium hydroxide. Addition of excess of 40% sodium hydroxide led, however, to separation of an oil which was evidently the sodium salt. This did not crystallize on cooling. Yield 72%.

Found %: N 5.46. C₁₂H₁₉O₂NS. Calculated %: N 5.80.

p-Aminobenzenesulfonyl sec.-butylamide (III) was prepared from 17.2 g (0.1 mole) of p-aminobenzenesulfamide and 0.2 mole of 2-butanol in 80% sulfuric acid (100 ml). Resinous substances (evidently polymers of butenes) were removed by extraction with 100 ml of dichloroethane; the sulfuric acid layer was diluted with water and neutralized with concentrated ammonia; a yellow oil came out and soon crystallized. The crystals were dissolved in a mixture of 20 ml of 40% sodium hydroxide and 70 ml of water with heating; to the filtered solution was added 40 ml of 40% sodium hydroxide; the sodium salt came down on cooling and was filtered off on a glass filter, and dissolved in water with addition of sodium hydroxide (for prevention of hydrolysis). Precipitation was then effected with saturated ammonium chloride solution. Yield 7.84 g (34.4%) with m.p. 120°. Crystallization from aqueous methanol gave needles with m.p. 120.5°.

Found %: N 12.16. C₁₀H₁₆O₂N₂S. Calculated %: N 12.27.

The product undergoes the diazo reaction: diazotization on paper with 2-naphthol to give an orange dye; with 1-naphthol an orange dye was also obtained, but wetting with alkali solution changed the color to magenta. The presence of a primary aromatic amino group was thereby established.

SUMMARY

The alkylation of arenesulfamides with 2-butanol in sulfuric acid solution was studied; it was found that N-monoalkyl derivatives of the arenesulfamides are formed. Alkylation of p-aminobenzenesulfamide with 2-butanol gave p-aminobenzenesulfonyl sec.-butylamide, i.e., alkylation proceeds only at the sulfamido group and the aromatic amino group is not alkylated.

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DOUBLE DIAZONIUM SALTS OF CHLORIDES OF BIVALENT COBALT AND COPPER

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Double diazonium compounds of cobalt have been described only in the patent literature [1]. As far as we are aware double diazonium salts of bivalent copper have never been described.

We prepared double diazonium salts of chlorides of copper and cobalt with the following aryldiazonium chlorides: benzene-, p-toluene-, p-chlorobenzene-, p-bromobenzene-, p-nitrobenzene-, and p-carbethoxybenzene. They are easily formed when cooled solutions of the aryldiazonium chlorides are brought into contact with the metal chlorides. Yields 55-80%. All of the investigated salts, with the exception of salts with p-bromobenzenediazonium, have 2 : 1 composition $[(ArN_2Cl)_2MeCl_2]$ regardless of the ratio of reactants and of the order of mixing; p-bromobenzenediazonium salts also have the 1 : 1 composition regardless of the order of mixing and the reactants ratio. All the double Cu^{2+} diazonium salts are yellow, while those of Co^{2+} are green-blue; they are readily soluble in water, moderately in alcohol, insoluble in ether; they do not have a sharp melting point; they decompose gradually when slowly heated and explode when rapidly heated.

Double diazonium salts of bivalent cobalt and copper are characterized by differing stabilities in the solid state and in solution. They are fairly stable in the solid state and can be stored without appreciable decomposition in a vacuum-desiccator over phosphorus pentoxide for several days $[(C_6H_5N_2Cl)_2COCl]_2$ to several months in the air $[(p-ClC_6H_4N_2Cl)_2CuCl_2]$. On the other hand the solutions of these salts are poorly stable: a solution in anhydrous alcohol starts to break down even at room temperature. The stability in solutions depends in large measure on the nature of the aromatic radical; for example, $(C_6H_5N_2Cl)_2CoCl_2$ and $(C_6H_5N_2Cl)_2CuCl_2$ in saturated alcoholic solution are completely decomposed with nitrogen evolution only after 2 hr, whereas $(p-NO_2C_6H_4N_2Cl)_2CuCl_2$ breaks down in the course of 1-2 min.

We took the infrared spectra in the $2100-2300\text{ cm}^{-1}$ region for the synthesized double diazonium salts of copper and cobalt. In Table 1 are set forth the results obtained for the absorption spectra in the solid state in the form of a paraffin oil paste. The table includes comparative data for the initial aryldiazonium chlorides.

We see from these data that the absorption of the cobalt and copper salts in the $2100-2300\text{ cm}^{-1}$ region due to the $N \equiv N$ bond has the features characteristic of double diazonium salts of other metals [2], i.e., the bands are lower than those of the corresponding aryldiazonium chlorides and the displacement is within the usual limits. The absorption band is complex - two peaks or lack of symmetry.

We investigated the electronic spectra of double diazonium salts of copper and cobalt chlorides with benzene-diazonium, p-toluenediazonium, and p-chlorobenzenediazonium chlorides in methanol solution. Results are set forth in Tables 2 and 3. In Table 2 the absorption characteristics of the initial aryldiazonium chlorides are included for comparison. The spectra of the double salts of p-toluenediazonium chloride with copper and cobalt chlorides are plotted in Fig. 1. The spectrum of p-toluenediazonium chloride itself, plotted in methanol, is included in the figure for comparison.

We see that in the ultraviolet region ($30,000-40,000\text{ cm}^{-1}$) the spectrum of the double diazonium salt retains the form characteristic of the aryldiazonium chloride itself. In the $10,000-30,000\text{ cm}^{-1}$ region the spectrum of the double diazonium salts of both copper and cobalt contains additional absorptor bands of medium intensity. It should be noted that the band characteristic of aryldiazonium cations is also retained in the spectra of double diazonium salts of other metals. We investigated [3] the electronic spectra of double diazonium compounds of salts of zinc,

TABLE 1. Absorption Maxima of the $N \equiv N$ Triple Bond of Double Diazonium Salts of Bivalent Copper and Cobalt (Paste in paraffin oil)

MeCl ₂	ArN ₂ Cl					
	p-CH ₃ C ₆ H ₄ N ₂ Cl	p-ClC ₆ H ₄ N ₂ Cl	p-BrC ₆ H ₄ N ₂ Cl	p-C ₆ H ₄ N ₂ Cl	p-NO ₂ C ₆ H ₄ N ₂ Cl	p-C ₆ H ₄ OOCC ₆ H ₄ N ₂ Cl
CoCl ₂	2256	2263	2248 •	2264	2271 2291	2272 2297
CuCl ₂	2247 (2257)	2260 2250	2253 •	2273 2259	••	2291
ArN ₂ Cl	2281	2277	2267	2294	2301	2295

• 1 : 1 composition.

•• The spectrum could not be plotted due to the great instability of the compound.

cadmium, mercury, and antimony with benzene-, p-toluene, and p-chlorobenzenediazonium compounds and satisfied ourselves that the spectra of these salts resembled the spectrum of the initial compound. Anderson and Steedly [4] similarly established the similarity between the spectra of double salts of zinc, mercury, and antimony with p-aminobenzenediazonium and its N-aryl-, N-acyl-, N-dialkyl-, and N-alkyl-N-acyl derivatives on the one hand and the spectra of the initial compounds on the other. We may therefore assume that the absorption bands developed in the spectrum of double diazonium salts of cobalt and copper in the 10,000-30,000 cm^{-1} region are associated with the nature of the metal.

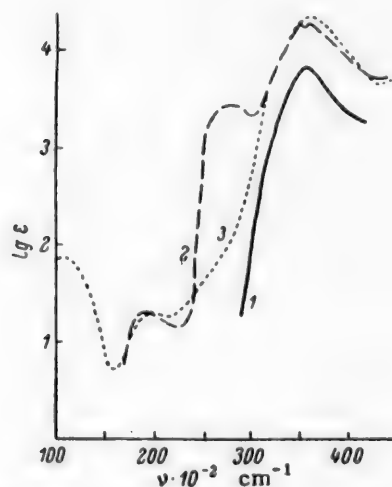


Fig. 1. Electronic absorption spectra in methanol. 1) $p\text{-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl}$; 2) $p\text{-CH}_3\text{-C}_6\text{H}_4\text{N}_2\text{Cl})_2 \cdot \text{CoCl}_2$; 3) $(p\text{-CH}_3\text{-C}_6\text{H}_4\text{N}_2\text{Cl})_2 \text{CuCl}_2$.



Fig. 2. Electronic absorption spectra. 1) $(p\text{-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{CuCl}_2$ in CH_3OH ; 2) $(p\text{-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{CuCl}_2$ in $\text{CH}_3\text{OH} + \text{HCl}$; 3) CuCl_2 in CH_3OH ; 4) CuCl_2 in $\text{CH}_3\text{OH} + \text{HCl}$.

TABLE 2. Electronic Absorption Spectra of Bivalent Cobalt Salts in Alcohol and in Alcohol Containing Hydrochloric Acid

Solvent Compound	CH ₃ OH					CH ₃ OH + HCl			Remarks
	CoCl ₂	I	I + CoCl ₂	II	II + CoCl ₂	III	III + CoCl ₂	CoCl ₂	
$\nu \cdot 10^{-3} (\lg \epsilon)$	15.2 (0.09)							14.5 (2.57) 15.2 (2.56)	Absorption characterizing the (CoCl ₂) ⁻² anion
	19.1 (0.90)	20.2 (2.09)			19.2 (1.32)		19.4 (1.27)	18.9 (0.81)	Absorption associated within the d-shell of the cobalt ion
		38.5 (3.83)	27.0 (2.13) 38.9 (4.18)	36.4 (3.79)	27.8 (3.43) 36.8 (4.28)	35.7 (4.20)	27.6 (3.14) 35.7 (4.41)	38.5 (4.16) 35.7 (4.28) 35.7 (4.51)	Absorption due to the diazo action

Note: I) C₆H₅N₂Cl; II) p-CH₃C₆H₄N₂Cl; III) p-ClC₆H₄N₂Cl.

TABLE 3. Electronic Absorption Spectra of Salts of Bivalent Copper in Solution in Alcohol and in Hydrochloric Acid-Containing Alcohol

Solvent Compound	CH ₃ OH					CH ₃ OH + HCl			Remarks
	CuCl ₂	I + CuCl ₂	II + CuCl ₂	III + CuCl ₂	CuCl ₂	I + CuCl ₂	II + CuCl ₂	III + CuCl ₂	
$\nu \cdot 10^{-3} (\lg \epsilon)$	10.5 (1.78)	10.5 (1.75)	10.5 (1.86)	10.5 (1.79)	10.5 (1.94)	10.5 (2.00)	10.5 (1.65)	10.5 (1.90)	Absorption due to electronic transitions inside the d-shell of the copper ion
		20.4 (1.06)	20.4 (1.31)	19.2 (1.79)		24.7 2.31	24.1 (2.16)	25.0 (2.56)	Absorption due to the (CuCl ₂) ⁻² ion
	38.5 (3.20)	39.2 (4.18)	36.4 (4.38)	35.7 (4.34)	25.3 (2.90) 35.1 (3.67)	38.5 (4.39)	35.1 (4.20)	35.7 (4.66)	Absorption due to the diazo cation

Note: I) C₆H₅N₂Cl; II) p-CH₃C₆H₄N₂Cl; III) p-ClC₆H₄N₂Cl.

We know from the chemistry of complex compounds that ions of metals whose d-shells are not filled differ from ions of metals with filled d-shells in absorbing in the visible region. The character of this absorption changes after complex formation, and also on change in the addends. We can therefore attempt to clarify the problem of the direct encirclement of the metal in double diazonium salts on the basis of the spectra of the double diazonium salts of copper and cobalt. If the double diazonium compounds of cobalt and copper have an ionic structure, i. e., $(\text{ArN}_2\text{Cl})^+[\text{MeCl}_4]^{2-}$, we should expect the absorption in the spectra of these compounds to be associated with the diazo cation and the complex $[\text{MeCl}_4]^{2-}$.

We see from Fig. 1 that the diazo cation is clearly represented in the spectra of double diazonium salts.

With the objective of clarifying the nature of the absorption of double diazonium salts of copper and cobalt in the 10,000-30,000 cm^{-1} region, we studied the changes taking place in the spectra of these compounds and in the spectra of copper and cobalt chlorides themselves in solution in alcoholic alone and in hydrochloric acid-containing alcohol. Results of these measurements are set forth in Tables 2 and 3. The corresponding spectra of the double salts with p-toluenediazonium chloride are plotted in Figs. 2 and 3.

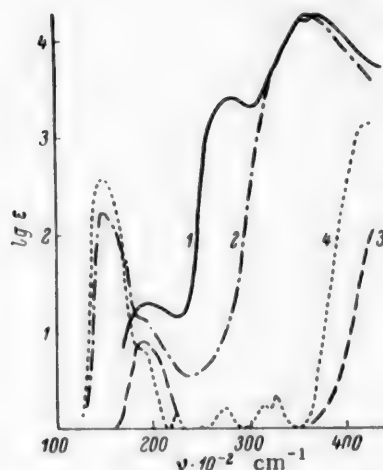


Fig. 3. Electronic absorption spectra. 1) $(\text{p-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{CoCl}_2$ in CH_3OH ; 2) $(\text{p-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{CoCl}_2$ in $\text{CH}_3\text{OH} + \text{HCl}$; 3) CoCl_2 in CH_3OH ; 4) CoCl_2 in $\text{CH}_3\text{OH} + \text{HCl}$.

spectra either in methyl alcohol or in methyl alcohol + hydrochloric acid. This band disappears in the spectra of solutions in methyl alcohol + hydrochloric acid and at the same time a band is developed in the 25,000 cm^{-1} region which is characteristic of absorption of the $[\text{CuCl}_4]^{2-}$ ion. Absorption in the 20,000 cm^{-1} region is observed in amine complexes of copper [8].

The following interpretation may be placed on the experimental results: The electronic spectra of double diazonium salts of cobalt and copper clearly reflect the presence of the diazocation in all solvents, whereas the absorption characterizing the $[\text{MCl}_4]^{2-}$ ion is developed only in solution in methyl alcohol + hydrochloric acid. The band observed in methyl alcohol solution in the 27,000 cm^{-1} region for cobalt salts and in the 20,000 cm^{-1} region for copper salts characterizes another "non-ionic" structure of the double diazonium salts of cobalt and copper. The disappearance of this absorption in hydrochloric acid solutions and the simultaneous appearance of a band characterizing the $[\text{MCl}_4]^{2-}$ anion show that the "non-ionic" structure is unstable and breaks down easily under the action of hydrochloric acid. We can confidently assert that in hydrochloric acid solutions the double diazonium salts are dissociated since the absorption corresponds to the diazocation $[\text{ArN}_2]^+$ and the $[\text{MCl}_4]^{2-}$ anion.

* Kiss [5] demonstrated the possibility in principle of recording of the absorption of the $[\text{MeCl}_4]^{2-}$ anion in the case of cobalt. Evidence was similarly adduced by Yatsimirskii [6] for copper in hydrochloric acid solutions.

TABLE 4. Double Diazonium Salts of Copper (p-XC₆H₄N₂Cl)_mCuCl₂

X	Empirical formula	% C		% H	
		found	calc.	found	calc.
H	C ₁₂ H ₁₀ N ₄ Cl ₄ Cu	34.38, 34.44	34.67	2.59, 2.65	2.42
CH ₃	C ₁₄ H ₁₄ N ₄ Cl ₄ Cu	37.78, 37.69	37.90	3.49, 3.60	3.18
Cl	C ₁₂ H ₈ N ₄ Cl ₆ Cu	30.09, 30.14	29.94	1.89, 1.99	1.66
Br	C ₆ H ₄ N ₂ Cl ₃ BrCu	20.17, 20.34	20.36	0.99, 1.06	1.13
C ₂ H ₅ OOCC	C ₁₈ H ₁₈ O ₄ N ₄ Cl ₄ Cu	38.29, 38.26	38.62	3.14, 3.17	3.24

TABLE 5. Double Diazonium Salts of Cobalt (p-XC₆H₄N₂Cl)_mCoCl₂

X	Empirical formula	% C		% H	
		found	calc.	found	calc.
H	C ₁₂ H ₁₀ N ₄ Cl ₄ Co	35.20, 35.34	35.06	2.23, 2.44	2.45
CH ₃	C ₁₄ H ₁₄ N ₄ Cl ₄ Co	38.08, 38.26	38.30	2.94, 3.02	3.21
Cl	C ₁₂ H ₈ N ₄ Cl ₆ Co	30.31, 30.25	30.15	1.86, 1.88	1.68
Br	C ₆ H ₄ N ₂ Cl ₃ BrCo	20.36, 20.45	20.63	1.15, 1.11	1.15
C ₂ H ₅ OOCC	C ₁₈ H ₁₈ O ₄ N ₄ Cl ₄ Co	38.63, 38.65	38.44	3.43, 3.48	3.26
NO ₂	C ₁₂ H ₈ O ₄ N ₆ Cl ₄ Co	28.58, 28.68	28.17	1.62, 1.67	1.60

The results of the present and the preceding [2] investigations shows that the structure of double diazonium salts both in the solid state and in solutions is not as simple as had hitherto been assumed. The hypothesis that a direct, although relatively weak, bonding of the metal with the nitrogen atom of the diazonium group is possible is supported by the dependence of the absorption band of the N ≡ N bond on the metal and its valence in the case of the solid compounds, and on the development in solutions of copper and cobalt salts of an absorption similar to that of corresponding compounds whose complex grouping contains a nitrogen atom.

EXPERIMENTAL

Spectra. The infrared spectra were obtained with a single-beam IKS-12 spectrophotometer with a lithium fluoride prism. Specimens were prepared in the form of a thick suspension in paraffin oil. The ultraviolet spectra were obtained with a SF-4 spectrophotometer.

Spectra of solutions of double diazonium salts of Cu²⁺ and Co²⁺, due to their great instability in dilute solutions, were obtained in the following manner: A solution of CuCl₂ or CoCl₂ of the necessary concentration was made up in anhydrous alcohol, and a solution of aryldiazonium chloride in anhydrous alcohol was separately made up in double the concentration (since the double diazonium salts of Cu²⁺ and Co²⁺ have 2 : 1 composition). Equal volumes of the two solutions (about 1.5 ml of each) were then mixed in the spectrophotometer cell, the latter was inserted in the instrument, and the spectra plotted. The duration of preparation of the solutions was not more than 15 sec, and the spectra were taken in not more than one minute. A fresh solution was then prepared by the above method.

Synthesis of preparations. Double diazonium salts of bivalent copper and cobalt are easily prepared by running together cooled alcoholic solutions of aryldiazonium chlorides and metal chlorides. The aryldiazonium chloride was prepared in anhydrous methanol. A cooled, saturated solution of cobalt or copper chloride in anhydrous methanol was stirred into a solution (cooled to -10°) of aryldiazonium chloride in the minimum quantity of methanol. Solutions were prepared with molar ratios of 2 : 1, i.e., 0.01 mole of aryldiazonium chloride and 0.005 mole of metal chloride. Crystals of the double salt came down immediately (or sometimes after a short period) when the solutions were mixed. Yield 55-80%. The precipitate was quickly filtered off and washed twice with cooled anhydrous methanol and absolute ether. The double salt was dried in a vacuum-desiccator over phosphorus pentoxide. Analyses of the prepared double diazonium salts of copper and cobalt are set forth in Tables 4 and 5.

SUMMARY

1. Double diazonium salts of chlorides of cobalt and copper were prepared with benzene-, p-chlorobenzene-, p-bromobenzene-, toluene-, p-nitrobenzene-, and p-carbethoxybenzenediazonium chlorides.
2. The infrared spectra of these salts were studied in the solid state in the region of the $N \equiv N$ valence vibrations.
3. The electronic spectra were studied in solutions in methyl alcohol and methyl alcohol + hydrochloric acid.
4. The hypothesis of bonding of metal with the nitrogen of the diazonium group in molecules of double diazonium salts of Co^{2+} and Cu^{2+} is proposed on the basis of the electronic and vibrational spectra.

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INFRARED ABSORPTION SPECTRA OF DOUBLE SALTS
OF o- AND m-SUBSTITUTED ARYLDIAZONIUM
CHLORIDES WITH METAL CHLORIDES

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In the preceding publications [1-4] it was shown that the valence vibration frequencies of the $N \equiv N$ bond in double salts of metal chlorides and aryldiazonium chlorides with substituents in the para-position of the benzene ring $[(ArN_2Cl)_m(MCl_n)_p]$ depends on the character of the substituent, on the nature of the metal and its valence, and on the ratio of m to p.

In the present work we investigated double diazonium salts whose benzene ring contains substituents in the ortho- and meta-position. We also studied the infrared spectra in the 2100-2300 cm^{-1} region of compounds $XC_6H_4N_2Cl \cdot MCl_n$ where $X = o-CH_2O, o-CH_3, m-CH_3, o-Cl, o-COOC_2H_5, o-NO_2, m-NO_2$; $M = Zn^{2+}, Cd^{2+}, Pb^{4+}, Sb^{5+}, Cu^{2+}, Co^{2+}, Fe^{+3}$.

We obtained the spectra of the double diazonium salts in this region both for the solid compounds (paste in paraffin oil) and for the solutions in methanol. Results of measurements are set forth in Table 1. The compounds were synthesized by the methods described. Table 1 includes, for comparison, data relating to the corresponding aryldiazonium chlorides and borofluorides, as well as data for double salts of benzenediazonium chloride itself taken from an earlier paper [1].

We see from Table 1 that in methanol solutions the position of the $N \equiv N$ absorption maximum $\nu_{N \equiv N}$ for a given substituent is constant (within the limits of experimental error) in the case of aryldiazonium chlorides, their borofluorides, and the investigated double diazonium salts. Such an effect can only be explained on the assumption that the aryldiazonium chlorides, the borofluorides, and the double diazonium salts with chlorides of metals are dissociated in solution into the diazonium cation ArN_2^+ and the corresponding anion $[Cl^-, BF_4^-, (MCl_n + 1)^-]$. Averaged values of the $N \equiv N$ frequency for the respective diazocations are set forth in Table 1.

Table 2 is compiled on the basis of the present results and of the earlier investigations of the absorption in the 2100-2300 cm^{-1} region for solutions of aryldiazonium compounds in methanol. Substituents are arranged in order of increasing value of $\nu_{N \equiv N}$. This table shows that a definite regularity occurs in respect to the influence of substituents in the aromatic ring on the position of the absorption band of the triple bond: Electronegative substituents lower the frequency of the absorption band, while electropositive substituents increase it. The order of the substituents in the table ($CH_3O, CH_3, Cl, H, C_2H_5OOC, NO_2$) is also the order of decreasing electron-donating ability of the substituents. The $\nu_{N \equiv N}$ frequencies for aryldiazonium chlorides in the solid state retain the value characteristic of the diazocation; this is in harmony with the ionic structure of solid aryldiazonium chlorides which was revealed by x-ray analysis in the case of benzenediazonium chloride [5].

As far back as 1897, Hirsch [6] reported that difficultly crystallizable oils were very frequently obtained instead of crystalline compounds during synthesis of aryldiazonium compounds in presence of hydrochloric acid. He put forward the hypothesis that they were complex compounds of the diazonium chloride with hydrochloric acid of the type $ArN_2Cl \cdot nHCl$. Hantzsch [7] later reported the isolation of a series of such complexes.

During the synthesis of o-anisyl- and o-carbethoxybenzenediazonium chlorides in presence of hydrochloric acid we likewise obtained oils which very slowly crystallized over alkali in vacuo. During the crystallization period we recorded the infrared spectra in the 2100-2300 cm^{-1} (Fig. 1). The spectra of the oily products had an absorption band with a $\nu_{N \equiv N}$ frequency somewhat lower than that of the $\nu_{N \equiv N}$ of the corresponding diazocation. Continued maintenance of the oily product in vacuo over alkali led to the appearance in the spectra of a second band

TABLE 1. Maxima of Absorption of $\nu_N \equiv N$ in cm^{-1} for $(X\text{C}_6\text{H}_4\text{N}_2\text{Cl})_m(\text{MCl}_n)_p$

X	Medium	Value of m : p								Cl ⁻	BF ₄ ⁻	Cation (mean value for solutions)
		CuCl ₂		ZnCl ₂	CdCl ₂	PbCl ₂	SbCl ₃	FeCl ₃	CoCl ₂			
		1 : 1	2 : 1	2 : 1	2 : 1	2 : 1	1 : 1	1 : 1	2 : 1			
o-CH ₃	Paraffin oil CH ₃ OH	• 2256 2265	2263 2264	2262 Not soluble	2260 (2250) Not soluble	• 2239 (2219) 2254 2265	2247 (2228) 2260 2266	• 2260 2266	2260 2266	2248 2268	2266	
			• 2260 2274	2258 2270	2255 ¹ Not soluble		2254 2270	2242 2268		2266 2272		2288 2274
o-Cl	The same	• 2271 2282	2274 2281	2266 Not soluble	2272 Not soluble	2262 2283	2252 2283	• 2272 ¹ 2282	2278 2281	2293 2281	2282	
			• 2278 2292	• 2282 (2291) 2291	• 2279 ¹ 2292	• 2280 Not soluble	• 2268 ² 2291	• 2273 ² 2291	• 2282 (2289) 2296	2244 2292		2301 2293
o-NO ₂	The same	• 2271 2293 2298	2284 2298	2262 Not soluble	2281 Not soluble	2272 2298	2277 ² 2297	2285 2299	2278 2298	2298 2301	2299	
			• 2265 (2272) 2283	2268 2277	2267 Not soluble	2268 Not soluble		2263 2280	• 2268 ¹ 2281	2279 2278		2302 2289
m-CH ₃	The same		2291 2305	• 2291 2307	2284 Not soluble	2281 2304	2279 2301	• 2288 2295 2305	2306 2303	2306 2308	2304	
m-NO ₂	The same		• 2294 2278 2304									

Note: When the absorption band is unsymmetrical or split, the main frequency is followed by a second band or shoulder (the latter in brackets). Compounds prepared for the first time are indicated by asterisks. 1) Composition of products 1 : 1; 2) compounds obtained in the form of oils.

TABLE 2. Relation between $\nu_{N \equiv N}$ for ArN_2^+ and the Substituent in the Benzene Ring

$\nu_{N \equiv N}$	Substituent	$\nu_{N \equiv N}$	Substituent	$\nu_{N \equiv N}$	Substituent
2263	p-CH ₃ O	2282	o-Cl	2298	p-COOC ₂ H ₅
2266	o-CH ₃ O	2288	p-Cl	2299	o-NO ₂
2272	o-CH ₃	2290	H	2304	m-NO ₂
2273	p-CH ₃	2291	o-COOC ₂ H ₅	2308	p-NO ₂
2280	m-CH ₃				

whose position coincided with that of the corresponding diazocation. The intensity of the latter band increased with passage of time, while that of the first band decreased. Finally only one band remained for the solid compounds in the region of $N \equiv N$ triple bonds, and this band corresponded to that of the diazocation in character and position.

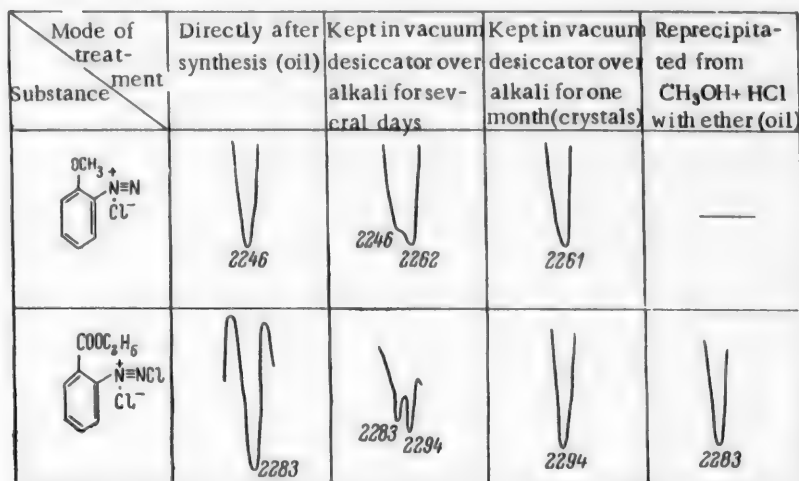


Fig. 1. Absorption spectra in the 2100-2300 cm^{-1} region of complex compounds of aryldiazonium chlorides with hydrogen chloride.

In order to demonstrate that the gradual change in the spectrum was associated with loss of the hydrogen chloride which had been bound in the form of a complex, we reprecipitated o-carboxybenzenediazonium chloride, which had been crystallized in a vacuum-desiccator over alkali, with ether from alcohol saturated with hydrogen chloride. This operation again led to formation of an oil whose spectrum was identical with that of the oily complex with hydrogen chloride* isolated directly from the reaction. Reprecipitation of the crystallized sample from pure alcohol

* Since the complex compounds $ArN_2Cl \cdot nHCl$ relatively easily lose HCl , we could not characterize them by analysis. The analysis of a specimen which had remained for a long period over alkali corresponded to o-carboxybenzenediazonium chloride.

did not change either its state of aggregation or the absorption band of the triple $N \equiv N$ bond. The hypothesis of Hirsch about the existence of complex compounds of aryldiazonium chlorides with hydrogen chloride is therefore also confirmed by the infrared spectra.

The results enable us to conclude that the frequency of the $N \equiv N$ bond absorption band changes not only on formation of double diazonium salts [1-4] or perhalides [8], but also on formation of complex compounds with hydrogen chloride. The lowering of the $N \equiv N$ frequency by 20 cm^{-1} observed for o-nitrobenzenediazonium chloride can evidently be regarded as the consequence of formation of such a complex.

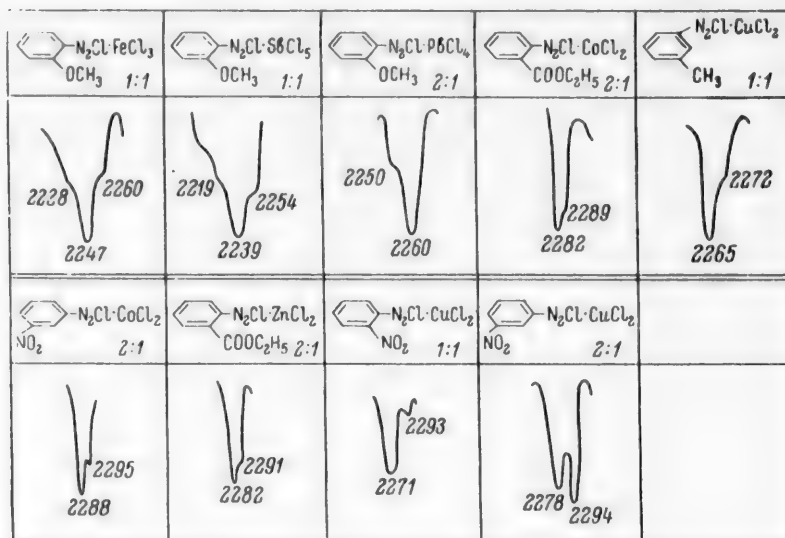


Fig. 2. Absorption spectra in the $2100\text{--}2300\text{ cm}^{-1}$ region of complex compounds of aryldiazonium chlorides with hydrogen chloride.

The double diazonium salts investigated in the present work, in the form of a paraffin oil paste, mainly have the same spectral characteristics of the triple $N \equiv N$ bond as the corresponding p-substituted salts which we studied earlier [1]. The position of their $N \equiv N$ absorption band thus depends to the same extent on the nature of the substituent in the aromatic ring and of the metal. A complex structure of the absorption band is observed in a series of cases for double salts of ortho- and meta-substituted benzenediazonium chlorides as well as for their para-analogs, although this spectral characteristic is less conspicuous. In Fig. 2 are plotted the absorption curves in the region of the triple bond valence vibrations of those double diazonium salts for which displacement or asymmetry of the bands had been observed. Only one symmetrical absorption band is observed for the remaining compounds investigated in the present work (including the chlorides and borofluorides).

The double diazonium salts of ferric chloride with o-nitro- and o-carbethoxybenzenediazonium compounds, also the salt of antimony pentachloride with o-carbethoxybenzenediazonium chloride, are isolated in the form of non-crystallizing oils. The spectra of solutions of these compounds in methanol exhibited the feature described above – the maximum of the absorption band of the triple $N \equiv N$ bond is the same as that of the corresponding diazocation; the $N \equiv N$ frequency of the oily compound itself is lowered by approximately the same amount as that of solid salts of the given metal with other aryldiazonium chlorides.

On the basis of the results set forth, we may suggest that the lowering of the triple bond vibration frequencies observed during formation of double diazonium salts is not governed by the characteristics of the crystal structure of these salts.

The maxima of the $\nu_{N \equiv N}$ absorption band of aryldiazonium borofluorides, measured in the solid state, are systematically lowered by $6\text{--}22\text{ cm}^{-1}$ (except for nitrobenzenediazonium compounds), whereas hitherto we have only encountered lowering of the $\nu_{N \equiv N}$ frequency in formation of complex diazonium compounds, which was fully consistent with the usual lowering of the valence vibration frequencies of groups directly linked to metal in complex compounds. The increase of the $\nu_{N \equiv N}$ frequency of borofluorides is evidently associated with their structural features.

EXPERIMENTAL

The absorption spectra were measured with a single-beam IKS-4 spectrophotometer with a lithium fluoride prism. The instrument was calibrated with the help of standard spectra of atmospheric moisture with carbon dioxide and gaseous hydrogen chloride. Specimens were prepared in the form of finely triturated substance in paraffin oil. Spectra of solutions were measured in dry methanol.

Diazo nitrogen was determined by the volumetric method of Rosenberger [9]. Aryldiazonium chlorides corresponding to o-anisidine, o- and m-toluidine, o-chloroaniline, o-carbethoxyaniline, and o- and m-nitroanilines were prepared by Knoevenagel's method. Borofluorides of the same aryldiazonium compounds were prepared by Starney's method [10].

Double salts of cadmium, zinc, and lead chlorides with o-anisylidiazonium, o- and m-toluenediazonium, o-chlorobenzenediazonium chlorides, also the salts $(m\text{-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{PbCl}_4$ and $(m\text{-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2\text{ZnCl}_4$, were prepared by the methods of A. N. Nesmeyanov and K. A. Kocheshkov [11].

The following salts of the metals in question, not previously described, were synthesized: $(o\text{-C}_2\text{H}_5\text{OOC}_6\text{H}_4\text{N}_2\text{Cl})_2\text{PbCl}_4$ lemon-yellow crystals, poorly soluble in water, decomp.p. 138°.

Found %: N 7.15, 7.40. $\text{C}_{18}\text{H}_{18}\text{O}_4\text{N}_4\text{Cl}_6\text{Pb}$. Calculated %: N 7.22.

$o\text{-C}_2\text{H}_5\text{OOC}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{CdCl}_2$: prepared by mixing equimolar quantities of an alcoholic solution of o-carbethoxybenzenediazonium chloride and a saturated aqueous solution of cadmium chloride. Colorless, stable, amorphous substance, readily soluble in water and alcohol. Decomp.p. 144-146°.

Found %: N 6.88, 7.01. $\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{Cl}_3\text{Cd}$. Calculated %: N 7.07.

$(o\text{-C}_2\text{H}_5\text{OOC}_6\text{H}_4\text{N}_2\text{Cl})_2\text{ZnCl}_2$: prepared like the preceding salt but with 2 : 1 ratio of diazonium chloride to zinc chloride. The compound came down in the form of an oil on precipitation with ether, and it crystallized in vacuo over phosphorus pentoxide. Similar in properties to the preceding salt. M.p. (decomp.) 105-106°.

Found %: N 9.93, 9.66. $\text{C}_{18}\text{H}_{18}\text{O}_4\text{N}_4\text{Cl}_4\text{Zn}$. Calculated %: N 9.96.

$(m\text{-NO}_2\text{C}_6\text{H}_4\text{N}_2\text{Cl})_2 \cdot \text{CdCl}_2$: prepared by running together an alcoholic solution of o-nitrobenzenediazonium chloride with a saturated aqueous solution of cadmium chloride in 1 : 2 molar ratio, followed by precipitation of the salt with ether. A colorless, stable substance without a definite decomposition point.

Found %: C 25.70, 26.88; H 1.74, 1.60. $\text{C}_{12}\text{H}_8\text{N}_6\text{O}_4\text{Cl}_4\text{Cd}$. Calculated %: C 25.99; H 1.45.

Double salts of ferric chloride with o-chloro- and o- and m-nitrobenzenediazonium chlorides, also with m-toluenediazonium chloride, were prepared by the procedure of A. N. Nesmeyanov and K. A. Kocheshkov [11].

$o\text{-CH}_3\text{OC}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{FeCl}_3$ was synthesized by the method of [12]. M. p. (decomp.) 102°C

Found %: N 8.47 $\text{C}_7\text{H}_7\text{ON}_2 \cdot \text{Cl}_4 \text{Fe}$. Calculated %: N 8.67

$o\text{-C}_2\text{H}_5\text{OOC}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{FeCl}_3$ was prepared like the preceding salt. A green, stable oil which failed to crystallize

Found %: N 7.45, 7.41. $\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{Cl}_4 \text{Fe}$. Calculated %: N 5.96.

The double salts of antimony pentachloride and o-chloro- and o- and m-nitrobenzenediazonium chlorides were prepared by O. A. Reutov's method [13].

$o\text{-ClC}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{SbCl}_5$, decomp.p. 160-162°.

Found %: N 5.66, 5.65. $\text{C}_6\text{H}_4\text{N}_2\text{Cl}_7\text{Sb}$. Calculated %: N 5.96.

New salts were prepared by the same procedure.

$o\text{-CH}_3\text{OC}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{SbCl}_5$: a stable, colorless, amorphous substance. It came down as an oil which solidified when rubbed. Decomp.p. 147-149°.

Found %: N 5.95, 5.80. $\text{C}_7\text{H}_7\text{ON}_2\text{Cl}_6\text{Sb}$. Calculated %: N 5.96.

$o\text{-CH}_3\text{C}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{SbCl}_5$: an unstable crystalline substance with a grayish tinge, very highly soluble in acetone. Decomp.p. 73-75°.

Found %: N 6.01, 6.08. $\text{C}_7\text{H}_7\text{N}_2\text{Cl}_6\text{Sb}$. Calculated %: N 6.17.

$o\text{-C}_2\text{H}_5\text{OOC}\text{C}_6\text{H}_4\text{N}_2\text{Cl} \cdot \text{SbCl}_5$: The brownish, unstable diazonium oil (from 0.01 M amine hydrochloride, 1.7 ml isoamyl nitrite, and 15 ml dry methanol in presence of a few drops of $\text{CH}_3\text{OH} + \text{HCl}$) was mixed at -5 to -10° with

TABLE 3. Double Diazonium Salts of Copper $(\text{XC}_6\text{H}_4\text{N}_2\text{Cl})_m\text{CuCl}_2$

X	m	Form	Fusion point with decomp.	Empirical formula	Diaz nitrogen content (%)	
					found	calc.
$o\text{-CH}_3\text{O}$	2	Yellow-orange crystals	119–120°	$\text{C}_{14}\text{H}_{14}\text{O}_2\text{N}_4\text{Cl}_4\text{Cu}$	11.73, 11.74	11.77
$o\text{-CH}_3$	2	Yellow unstable crystals	70	$\text{C}_{14}\text{H}_{14}\text{N}_4\text{Cl}_4\text{Cu}$	13.32, 13.20	12.62
$o\text{-Cl}$	1	Yellow crystals	103–105	$\text{C}_6\text{H}_4\text{N}_2\text{Cl}_4\text{Cu}$	9.25, 9.19	9.02
$o\text{-C}_2\text{H}_5\text{OOC}$	1	Black-green crystals	—	$\text{C}_9\text{H}_9\text{O}_2\text{N}_2\text{Cl}_3\text{Cu}$	8.13, 8.15	8.07
$o\text{-C}_2\text{H}_5\text{OOC}$	2	Yellow crystals	79–81	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{N}_4\text{Cl}_4\text{Cu}$	9.87, 10.00	10.05
$o\text{-NO}_2$	1	Light-yellow crystals	in alcohol 90 by explosion	$\text{C}_6\text{H}_4\text{O}_2\text{N}_3\text{Cl}_3\text{Cu}$	8.70, 7.79	8.75
$o\text{-NO}_2$	2	Yellow, rapidly darkening crystals	by explosion at 90°	$\text{C}_{12}\text{H}_8\text{O}_4\text{N}_6\text{Cl}_4\text{Cu}$	11.15, 11.05	11.08
$m\text{-CH}_3$	1	Yellow, unstable substance	at 90°	$\text{C}_7\text{H}_7\text{N}_2\text{Cl}_3\text{Cu}$	9.77, 9.86	9.68
$m\text{-NO}_2$	2	Yellow substance	69–70	$\text{C}_{12}\text{H}_8\text{O}_4\text{N}_6\text{Cl}_4\text{Cu}$	10.71, 10.92	11.08

TABLE 4. Double Diazonium Salts of Cobalt $(\text{XC}_6\text{H}_4\text{N}_2\text{Cl})_m\text{CoCl}_2$

X	m	Form	Fusion point (with decomp.)	Empirical formula	Diaz nitrogen content (%)	
					found	calc.
$o\text{-CH}_3\text{O}$	2	Blue-green crystals	140–141°	$\text{C}_{14}\text{H}_{14}\text{O}_2\text{N}_4\text{Cl}_4\text{Co}$	12.05, 11.98	11.90
$o\text{-Cl}$	1	Blue-green crystals	136–137	$\text{C}_6\text{H}_4\text{N}_2\text{Cl}_3\text{Co}$	9.00, 9.02	9.18
$o\text{-C}_2\text{H}_5\text{OOC}$	2	Blue-green crystals	102–103	$\text{C}_{18}\text{H}_{18}\text{O}_4\text{N}_4\text{Cl}_4\text{Co}$	10.01, 9.84	10.09
$o\text{-NO}_2$	2	Green crystals	129–131	$\text{C}_{12}\text{H}_8\text{O}_4\text{N}_6\text{Cl}_4\text{Co}$	11.31, 11.36	11.18
$m\text{-CH}_3$	1	Blue-green unstable crystals	80–90	$\text{C}_7\text{H}_7\text{N}_2\text{Cl}_3\text{Co}$	10.07, 10.05	9.84
$m\text{-NO}_2$	2	Green crystals	125–126	$\text{C}_{12}\text{H}_8\text{O}_4\text{N}_6\text{Cl}_4\text{Co}$	11.07, 11.11	11.18

a cooled, saturated methanolic solution of 0.005 or 0.01 M (in dependence on the composition of the resulting salt) copper chloride or cobalt chloride. The double salt usually came down immediately after the mixing of the components, or it was precipitated with ether. Oils separated in the cases of the o -carbethoxybenzenediazonium and o - and m -nitrobenzenediazonium compounds, and these crystallized on trituration and cooling. The crystals were washed with a mixture of alcohol and ether and then with ether, and dried in vacuo over phosphorus pentoxide. Yield 60–90%.

Cobalt salts were purified by recrystallization or by reprecipitation with ether from dry $\text{CH}_3\text{OH} + \text{HCl}$. Copper salts were recrystallized from $\text{CH}_3\text{OH} + \text{HCl} + \text{CuCl}_2$.^{*} Analyses and constants of the synthesized double compounds are set forth in Tables 3 and 4.

SUMMARY

1. The absorption of double diazonium salts with substituents in the ortho- and meta-positions is studied in the 2100-2300 cm^{-1} region. The frequency of the $\text{N} \equiv \text{N}$ valence vibrations, like that of the ortho-analogs, is shown to depend on the nature of the metal, on the substituent in the benzene ring, and on the ratio of components.
2. Absorption in the 2100-2300 cm^{-1} region of alcoholic solutions of the double salts is systematically investigated. It is shown that diazonium salts are dissociated in solution with formation of diazocations.
3. The position of the absorption band of the diazocations depends on the substituent in the benzene ring, electronegative substituents raising and electropositive substituents lowering the $\text{N} \equiv \text{N}$ frequency vibrations in comparison with the frequencies in the unsubstituted benzene ring. Substituents are arranged in the following sequence of increasing ability to raise the $\text{N} \equiv \text{N}$ frequency: CH_3O , CH_3 , Cl , H , COOC_2H_5 , NO_2 .
4. It is shown that formation of products of addition of hydrogen chloride to aryldiazonium chlorides leads to lowering of the $\text{N} \equiv \text{N}$ vibration frequencies in comparison with the initial aryldiazonium chlorides.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

* Good results for nitrogen determinations in double diazonium salts of copper were only obtained after reprecipitation with ether from $\text{CH}_3\text{OH} + \text{HCl} + \text{CuCl}_2$.

INVESTIGATIONS ON CONJUGATED SYSTEMS

CXLIII. THE DIRECTION OF HYDRATION OF ALKYLPHENYLACETYLENES

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The sequence of addition of water under the conditions of the Kucherov reaction to acetylenic hydrocarbons of various structures depends in great measure on their structure.

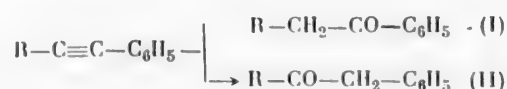
Monosubstituted acetylenes give only methylketones. Disubstituted acetylenes usually give approximately equal quantities of the two possible ketones. However, the presence of a tertiary butyl radical at the triple bond is accompanied by predominant formation of alkyl tertiary butyl ketone [1].

Water adds on to vinylacetylene with formation of methyl vinyl ketone. The sequence of addition of water is reversed if an acetylenic hydrogen is replaced by a methyl radical, and methyl propyl ketone is the predominant product. A further change occurs in the sequence of addition of water if one more methyl radical is attached to the vinyl group: hydroxyl joins on to the acetylenic carbon linked to the isopropenyl radical [2].

All these features of the direction of addition of water to acetylenic hydrocarbons might be explained in terms of the effect of kinetic factors during formation of an intermediate complex, and more especially the effect of steric hindrance.

In continuation of the systematic study of the hydration of acetylenic compounds, we carried out experiments on the addition of water to methyl-, ethyl-, propyl-, isopropyl-, and tertiary butylphenylacetylenes in presence of HgSO_4 or sulfuric acid.

Hydration of alkylphenylacetylenes can be expected to lead to formation of two types of ketones—alkylphenyl ketones (I) or alkylbenzyl ketones (II). The first direction of hydration was probable since alkylphenylacetylenes resemble isopropylmethylacetylene in structure.

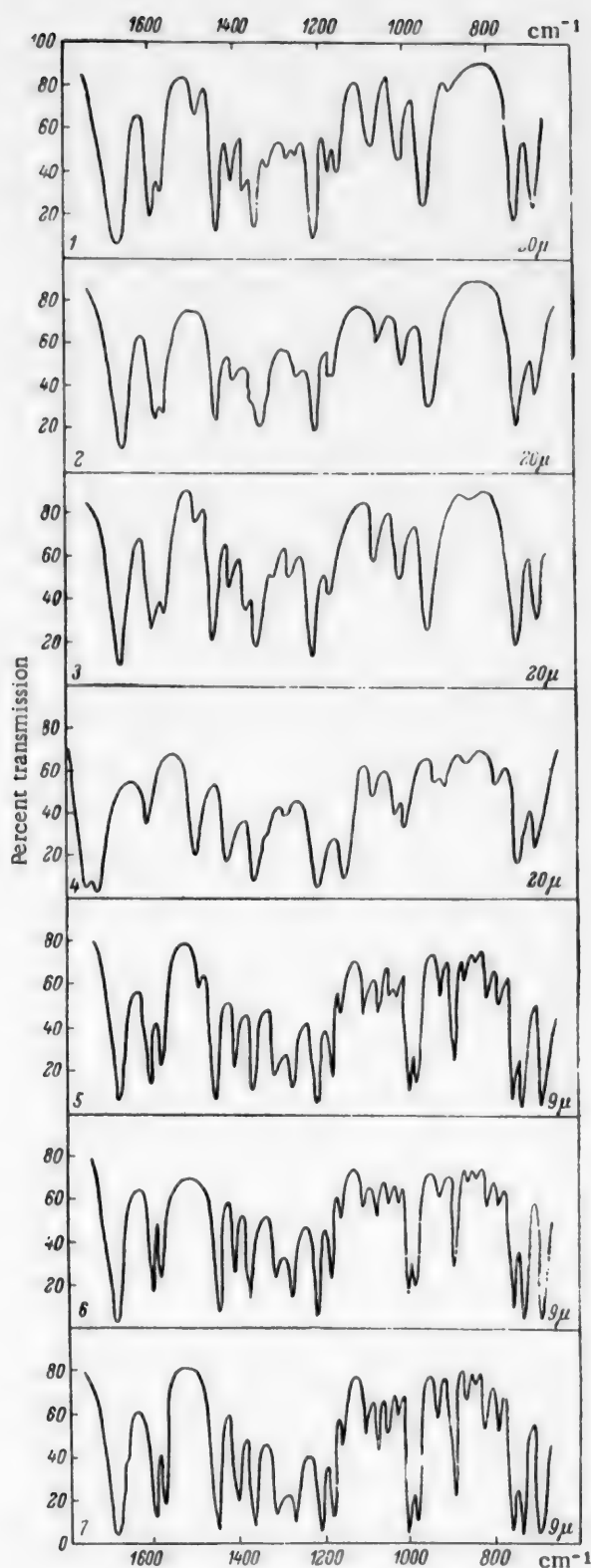


Experiments showed that in all cases alkylphenyl ketones are indeed formed (in a purer state in presence only of sulfuric acid).

The conclusions about the structure of the resulting ketones was based on comparison of their constants and infrared spectra with the corresponding data for authentic specimens. We had in our possession in two cases (methylphenyl and propylphenylacetylenes) both of the possible isomeric ketones.

The most essential differences in the infrared spectra of the isomeric ketones—possible products of hydration of alkylphenylacetylenes—are the consequence of ketones (I) containing a carbonyl group conjugated with the benzene ring which is associated with strong bands in the $1660-1690\text{ cm}^{-1}$ region, whereas ketones of type (II) contain an unconjugated carbonyl group and absorb at $1700-1760\text{ cm}^{-1}$. Due to the conjugation, the bands corresponding to the benzene ring are considerably weaker in the first case than in the second.

The isomeric ketones also differ considerably in respect to the character and intensity of absorption in the $900-1500\text{ cm}^{-1}$ region. Methyl benzyl ketone, for example, is characterized by extremely strong absorption bands at 1148 and 1492 cm^{-1} , which are associated with the presence of the acetyl and benzyl groupings. At the same time



the spectrum of ethyl phenyl ketone contains the strong 951 and 1378 cm^{-1} bands which are absent from the spectrum of the above-mentioned isomeric ketone (Fig. 1). Similarly propyl benzyl ketone absorbs strongly at 1492 cm^{-1} , butyl phenyl ketone at 967, 1180, 1250, and 1262 cm^{-1} (Fig. 2).

In all cases the infrared spectra of products of hydration of alkylphenylacetylenes in presence of H_2SO_4 are substantially indistinguishable from the spectra of authentic alkyl phenyl ketones. No appreciable intensification of absorption in the region of strong frequencies of other possible isomers was observed.

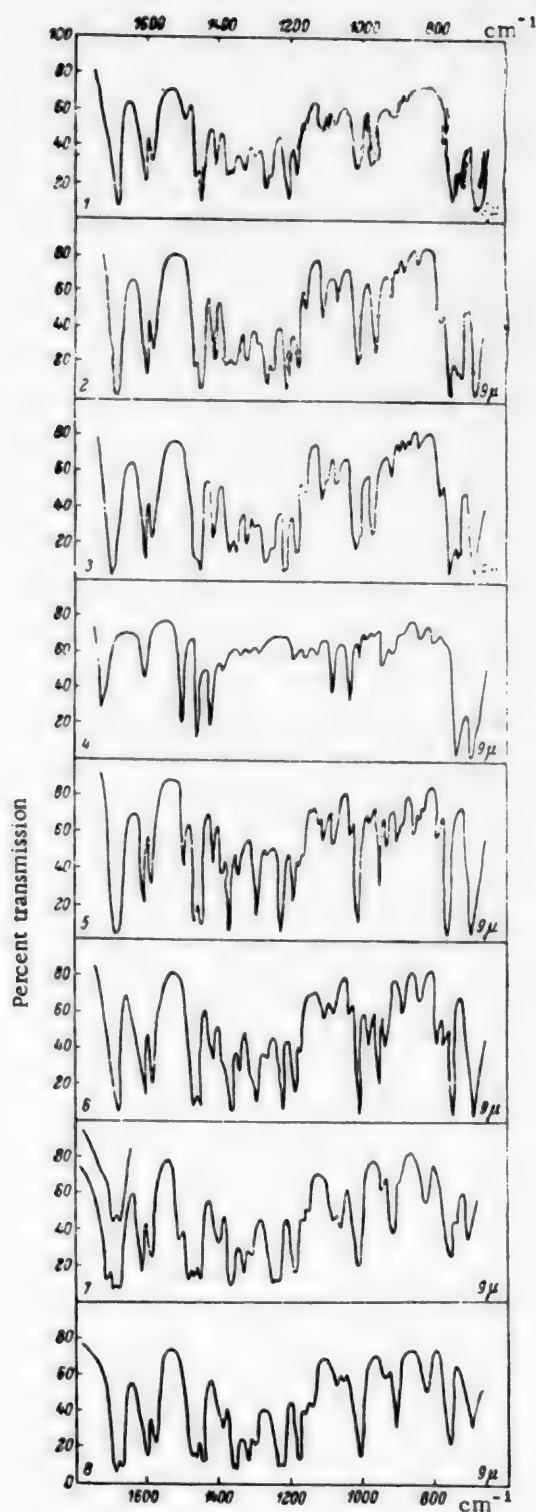
Hydration in presence of HgSO_4 gave ketones with the same structure but evidently not entirely free of the second possible isomer. They absorbed weakly in the 1700-1760 cm^{-1} region and also in the region of other strong frequencies of this isomer. In the infrared spectrum of the product of hydration of methylphenylacetylene, for example, there is a rise at about 1150 and 1490 cm^{-1} in comparison with an authentic sample. Examination of authentic mixtures of ethyl phenyl and methyl benzyl ketones showed that the content of impurity was less than 5%.

It has thus been demonstrated that the direction of addition of water to various alkylphenylacetylenes corresponds to the direction of hydration of isopropenylalkylacetylenes irrespective of the structure of the alkyl.

This law could be associated with the character of the electron density distribution in molecules of alkylphenylacetylenes or with the effect of steric factors.

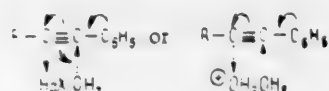
It may be postulated that an electron density shift represented by $\text{R}-\text{C}\equiv\text{C}-\text{C}_6\text{H}_5$, takes place in molecules of alkylphenylacetylenes since hydrocarbon radicals only function as electron donors while the phenyl radical can both repel and accept electrons. However the dipole moments of methylphenylacetylene

Fig. 1. Infrared transmission spectra. 1) Product of hydration of methylphenylacetylene in presence of mercuric sulfate; 2) product of hydration of methylphenylacetylene with 80% sulfuric acid; 3) ethyl phenyl ketone (sample); 4) methyl benzyl ketone (sample); 5) product of hydration of ethylphenylacetylene in presence of mercuric sulfate; 6) product of hydration of ethylphenylacetylene with 80% sulfuric acid; 7) propyl phenyl ketone (sample).



(0.37 D) and of *tert.* butylphenylacetylene (0.57 D)* were found to be smaller than the moments of methyl- and phenylacetylenes [3, 4]. This result may reflect the opposing effects of the two radicals at the triple bond.

The decisive effect on the polarization of molecules of alkylphenylacetylenes at the instant of reaction is most probably exerted not by the σ , π -conjugation of the triple bond with the methyl group, but the π , π -conjugation of the benzene ring with the triple bond which favors formation of a transition complex of the following type:



Steric factors evidently do not play important part since the structure of the alkyl radicals does not influence the sequence of addition of water.

EXPERIMENTAL

Methyl-, ethyl-, and propylphenylacetylenes were prepared by the action of the corresponding alkyl bromides on sodium phenylacetylide in liquid ammonia. *Tert.*butylphenylacetylene was prepared by the action of tertiary butyl bromide on phenylacetylenemagnesium bromide in ether. Yields of hydrocarbons were of the order of 50-60%. Isopropylphenylacetylene was prepared by the action of alcoholic KOH on the products of interaction of phenylisobutyl ketone with phosphorus pentachloride. Constants and analytical data for the hydrocarbons are given in Table 1, and the infrared spectra in Table 2 and Fig. 3.

* Determined in our laboratory by K. S. Mingaleva.

Fig. 2. Infrared transmission spectra. 1) Product of hydration of propylphenylacetylene in presence of mercuric sulfate; 2) product of hydration of propylphenylacetylene with 80% sulfuric acid; 3) butyl phenyl ketone (sample); 4) propyl benzyl ketone (sample); 5) product of hydration of isopropylphenylacetylene with 80% sulfuric acid; 6) phenyl isobutyl ketone (sample); 7) product of hydration of phenyl-*tert.*butylacetylene in presence of mercuric sulfate; 8) product of hydration of phenyl-*tert.*butylacetylene with 80% sulfuric acid.

TABLE 1. Constants of Alkylphenylacetylenes

Hydrocarbon	B.p.(pressure in mm)	d_4^{20}	n_D^{20}	Found, %		Gross formula	Calc., %	
				C	H		C	H
$C_6H_5-C\equiv C-CH_3$	72-73° (14)	0.9409	1.5638	—	—	—	—	—
$C_6H_5-C\equiv C-C_2H_5$	81-81.5 (10)	0.9209	1.5521	92.14, 92.10	7.86, 7.78	$C_{10}H_{10}$	92.26	7.74
$C_6H_5-C\equiv C-C_3H_7$	94-95 (10)	0.9096	1.5422	91.56, 91.43	8.53, 8.82	$C_{11}H_{12}$	91.61	8.39
$C_6H_5-C\equiv C-C_3H_7$ iso	88-89 (10)	0.9317	1.5420	—	—	—	—	—
$C_6H_5-C\equiv C-C_4H_9$ tert.	84 (10)	0.8778	1.5230	90.62, 90.83	9.04, 8.89	$C_{12}H_{14}$	91.09	8.91

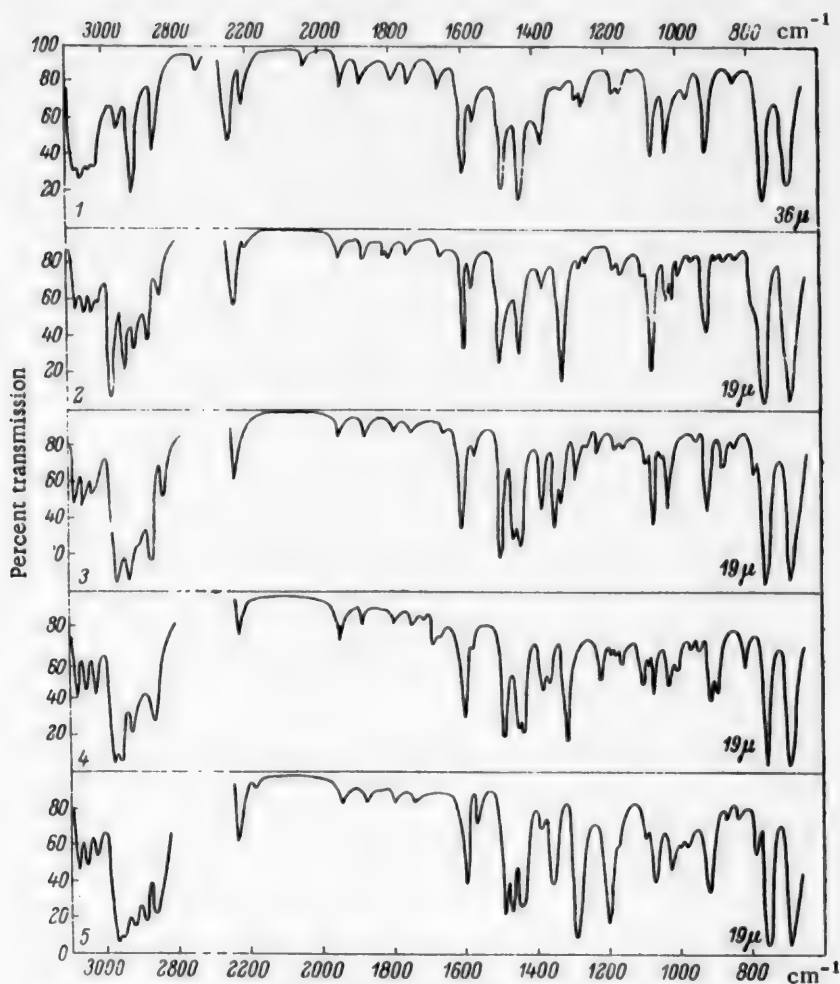


Fig. 3. Infrared transmission spectra. 1) Methylphenylacetylene; 2) ethylphenylacetylene; 3) propylphenylacetylene; 4) isopropylphenylacetylene; 5) tert.butylphenylacetylene.

TABLE 2. Infrared Spectra of Alkylphenylacetylenes

$\text{CH}_3\text{--C}\equiv\text{C--C}_6\text{H}_5$	$\text{C}_2\text{H}_5\text{--C}\equiv\text{C--C}_6\text{H}_5$	$\text{C}_3\text{H}_7\text{--C}\equiv\text{C--C}_6\text{H}_5$	iso $\text{--C}_4\text{H}_9\text{--C}\equiv\text{C--C}_6\text{H}_5$	$(\text{CH}_3)_2\text{C--C}\equiv\text{C--C}_6\text{H}_5$
631 s.	688 v.s.	687 v.s.	690 v.s.	688 v.s.
752 v.s.	752 v.s.	752 v.s.	752 v.s.	753 v.s.
—	784 m.	784 m.	—	785 m.
833 w.	835 w.	840 w.	845 m.	835 w.
—	872 w.	877 m.	892 m.	875 w.
912 s.	912 s.	912 s.	910 m.	912 m.
968 w.	960 w.	950 w.	940 w.	—
—	995 w.	—	962 w.	962 w.
—	1011 m.	—	1000 w.	985 w.
1026 s.	1027 m.	1025 s.	1025 m.	1027 m.
1066 s.	1067 s.	1068 s.	1068 m.	1067 m.
—	—	—	1087 w.	—
1129 v.w.	1093 w.	1090 w.	1098 m.	1097 w.
1154 w.	1155 w.	1155 w.	1155 w.	—
1169 w.	1175 w.	1175 w.	1175 w.	1175 w.
—	—	1224 w.	1216 m.	1200 s.
1262 w.	1255 w.	1253 w.	—	—
1274 w.	1274 w.	1284 m.	—	1288 v.s.
1319 v.w.	1317 s.	1325 s.	1317 s.	—
—	—	1337 s.	1360 m.	1360 s.
1375 m.	1374 m.	1380 s.	1380 m.	1388 w.
1434 v.s.	1437 s.	1440 s.	1440 s.	1443 s.
—	1450 m.	1457 s.	1450 s.	—
—	—	—	—	1474 s.
1483 v.s.	1487 s.	1487 s.	1488 s.	1487 s.
—	1572 m.	1565 w.	1574 w.	1572 w.
1598 v.s.	1598 s.	1598 w.	1595 s.	1597 m.
1663 w.	1660 w.	1655 w.	1683 w.	1635 w.
1744 w.	1752 w.	1744 w.	1740 w.	1747 w.
1795 w.	1818 w.	1795 w.	1792 w.	1800 w.
1878 w.	1875 w.	1872 w.	1882 w.	1875 w.
1940 w.	1945 w.	1947 w.	1947 w.	1947 w.
2038 w.	—	—	—	2187 w.
2208 m.	2206 w.	—	—	—
2240 s.	2235 w.	2235 m.	2227 w.	2237 m.
2736 w.	2842 w.	2935 m.	—	2865 s.
2853 s.	2876 s.	2970 s.	2868 s.	2898 s.
2917 v.s.	2912 s.	2900 s.	—	2922 s.
—	2936 s.	2930 v.s.	2925 s.	2946 v.s.
2953 m.	2976 v.s.	2963 v.s.	2968 v.s.	2972 v.s.
—	3020 m.	3011 m.	—	3024 m.
3034 s.	3032 m.	3032 m.	3030 w.	—
3053 s.	3051 m.	3056 m.	3056 w.	3055 m.
3074 s.	3077 m.	3080 m.	3080 w.	3080 m.

Note: v.s. = very strong, w. = weak, v.w. = very weak, m. = medium, s. = strong.

Hydration in presence of HgSO_4 . The hydrating mixture (3 g HgO , 26 g conc. H_2SO_4 , and 200 ml H_2O) was placed in a three-necked flask equipped with reflux condenser, stirrer, and dropping funnel. Dropwise addition was then made at 80° (in the case of methylphenylacetylene at 60°) in the course of 30 min of 0.1 mole of the hydrocarbon. Stirring was continued for another 4 hr at the same temperature, after which the reaction mixture was distilled with steam. The lower layer of distillate was collected, dried with calcined magnesium sulfate, and fractionated. Yields of ketones were 40-50% on the hydrocarbon taken. Part of the hydrocarbon was recovered.

Hydration in presence of H_2SO_4 . A mixture of 0.1 mole of hydrocarbon and 40 ml of 80% H_2SO_4 was shaken for 30 min. Reaction products were isolated by the preceding method.

Experimental results are compared in Table 3 and the infrared spectra of the ketones in Figs. 1 and 2. Frequencies of products of hydration of methylphenylacetylene and of specimens of all the expected ketones are given in Table 4.

TABLE 3. Hydration of Alkylphenylacetylenes

Hydrocarbon	Hydra- tion cat- alyst	Yield, %	B.p. (pressure in mm)	d_4^{20}	n_D^{20}
$\text{CH}_3\text{-(C}\equiv\text{C-C}_6\text{H}_5$	HgSO_4	50	212–214° (760)	1.0125	1.5259
	H_2SO_4	45	212–214 (760)	1.0131	1.5281
$\text{C}_2\text{H}_5\text{-(C}\equiv\text{C-C}_6\text{H}_5$	HgSO_4	52	113–115 (16)	0.9906	1.5194
	H_2SO_4	56	114–115 (16)	0.9897	1.5202
$\text{C}_3\text{H}_7\text{-(C}\equiv\text{C-C}_6\text{H}_5$	HgSO_4	50	113–114 (8)	0.9743	1.5149
	H_2SO_4	58	113–113.5 (8)	0.9744	1.5148
<i>iso</i> - $\text{C}_3\text{H}_7\text{-(C}\equiv\text{C-C}_6\text{H}_5$	H_2SO_4	50	108–109 (10)	0.9694	1.5122
<i>tert</i> - $\text{C}_4\text{H}_9\text{-(C}\equiv\text{C-C}_6\text{H}_5$	HgSO_4	44	109–110 (11)	0.9532	1.5078
	H_2SO_4	40	109–110 (11)	0.9541	1.5083

TABLE 4. Infrared Transmission Spectra of Ketones (cm^{-1})

Products of hydration of methylphenyl-acetylene in presence of		Ethyl phenyl ketone*	Methyl benzyl ketone*	Propyl phenyl ketone	Butyl phenyl ketone	Propyl benzyl ketone	Isobutyl phenyl ketone
HgSO_4^*	H_2SO_4^*						
694 s.	690 s.	690 s.	692 v.s.	690 v.s.	691 v.s.	698 v.s.	690 v.s.
744 v.s.	745 v.s.	744 v.s.	738 s.	736 s.	735 s.	735 v.s.	—
—	—	—	—	755 s.	753 v.s.	—	750 v.s.
—	—	—	—	—	—	—	772 m.
781 w.	784 w.	781 w.	784 w.	790 m.	782 m.	—	787 m.
815 w.	815 w.	815 w.	810 w.	820 m.	—	802 w.	835 w.
842 w.	845 w.	842 w.	845 w.	843 w.	843 w.	837 w.	—
897 w.	—	—	880 w.	868 w.	882 w.	890 v.w.	880 w.
—	—	—	913 w.	893 s.	—	—	—
—	934 w.	—	932 w.	932 m.	917 w.	913 w.	930 m.
951 s.	950 s.	951 s.	—	988 s.	967 s.	940 w.	947 m.
1003 m.	1003 w.	1002 m.	1002 w.	1000 s.	1002 m.	1002 w.	1006 s.
1010 m.	1014 w.	1011 m.	1028 s.	1025 w.	1012 s.	1030 m.	1025 w.
—	—	—	—	1050 w.	—	—	—
1076 m.	1078 s.	1074 m.	1075 m.	1075 m.	1075 m.	1077 w.	1073 w.
—	1100 w.	—	—	1101 m.	1109 m.	1116 w.	1095 m.
1157 m.	1160 m.	1157 w.	1157 v.s.	1158 m.	1159 m.	1153 w.	1157 m.
1180 m.	1180 s.	1180 m.	—	1180 s.	1180 s.	1182 w.	1180 s.
—	—	—	1206 v.s.	—	—	1202 w.	—
1217 v.s.	1220 v.s.	1218 v.s.	1221 v.s.	1215 v.s.	1210 v.s.	—	1212 v.s.
1264 m.	1265 m.	—	—	—	1250 s.	—	1258 m.
1276 m.	1280 m.	1278 m.	1290 s.	1272 s.	1262 s.	1273 w.	1285 m.
1300 m.	1300 m.	1305 w.	—	—	1295 m.	1305 w.	1302 m.
1320 m.	1320 m.	1322 m.	1320 w.	1315 s.	1320 s.	1327 w.	1333 m.
—	—	—	—	—	1345 s.	—	—
1350 v.s.	1347 v.s.	1352 v.s.	1357 v.s.	1368 s.	1360 s.	1361 w.	1366 s.
1376 s.	1377 s.	1378 s.	—	—	1377 s.	1360 m.	1378 w.
—	—	—	—	1408 s.	1410 s.	1413 s.	1405 w.
1411 m.	1413 s.	1414 s.	1422 v.s.	—	—	—	—
1449 s.	1449 s.	1449 s.	1449 s.	1450 v.s.	1449 v.s.	1452 s.	1446 s.
1493 w.	1490 w.	1489 w.	1494 s.	—	1460 s.	—	1460 s.
—	—	—	—	—	—	1492 s.	—
1583 s.	1582 s.	1584 s.	1588 w.	1580 s.	1580 s.	1580 w.	1578 s.
1596 s.	1598 s.	1598 s.	1602 s.	1597 s.	1596 s.	1601 s.	1595 s.
1677 v.s.	1677 v.s.	1676 s.	—	1685 v.s.	1680 v.s.	—	1678 v.s.
1700 m.	—	—	1705 v.s.	—	—	1705 v.s.	—
—	—	—	1750 s.	—	—	—	—

Note: v.s. = very strong, w. = weak, v.w. = very weak, m. = medium, s. = strong.

Note: The spectra of compounds marked with an asterisk were plotted with the IKS-14 spectrophotometer, the remainder with the IKS-15 instrument.

TABLE 5. Constants of Authentic Alkyl Phenyl and Alkyl Benzyl Ketones [7]

Ketone	B.p. (pressure in mm)	d_4^{20}	n_D^{20}
$C_6H_5-CO-CH_2-CH_3$	212–213° (760)	—	1.5275
$C_6H_5-CH_2-CO-CH_3$	212–215 (760)	1.0143	1.5160
$C_6H_5-CO-CH_2-CH_2-CH_3$	113–113.5 (15)	0.9885	1.5202
$C_6H_5-CO-CH_2-CH_2-CH_2-CH_3$	113–113.5 (8)	0.9744	1.5252
$C_6H_5-CH_2-CO-CH_2-CH_2-CH_3$	129 (10)	—	1.5198
$C_6H_5-CO-CH_2-CH(CH_3)_2$	108–109 (10)	0.9687	1.5120

Authentic alkyl phenyl ketones were prepared by acylation of benzene with the chlorides of the corresponding acids in presence of $AlCl_3$. Methyl benzyl ketone was prepared by heating a mixture of phenylacetic acid, acetic anhydride, and sodium acetate on an oil bath for 20 hr [5]. Propyl benzyl ketone was prepared by the action of propylmagnesium bromide on phenylacetonitrile in ether [6].

Constants of the authentic alkyl phenyl and alkyl benzylketones are set forth in Table 5.

SUMMARY

1. The hydration of methyl-, ethyl-, propyl-, isopropyl-, and tert.butylphenylacetylenes in presence of sulfuric acid or mercuric acid is investigated.
2. It is shown that in both cases the reaction products are alkyl phenyl ketones.
3. Possible causes of the direction of the reaction are discussed.

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REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENIC HYDROCARBONS

VII. REACTION OF 1-CHLORO-5-METHYL-, 1,3-DICHLORO-5-METHYL- AND 1-CHLORO-3,5-DIMETHYL-2,6-OCTADIENES WITH SODIUM ACETYLACETONE

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In our laboratory we previously studied the exchange reactions of some chlorine-containing telomers of dienic hydrocarbons with sodium ethylacetoacetate and sodium diethyl malonate [1,2]. In continuation of these investigations we have studied the reaction with sodium acetylacetonate of the primary products of telomerization of 1,3-butadiene, chloroprene, and isoprene (2-methyl-1,3-butadiene) with piperylene (1,3-pentadiene) hydrochloride.

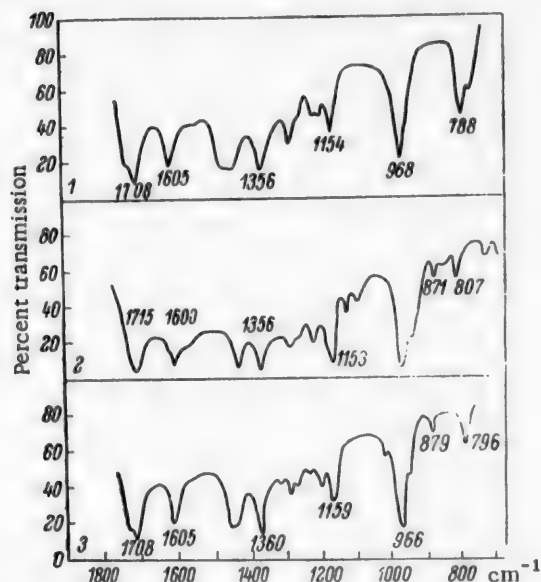
The experiments showed that the products of this reaction in a medium of anhydrous acetone are β -ketones of type (A). Allylic isomers of type (B), whose formation could have been expected in view of the allylic character of the chlorine atom in the telomer molecules, were not detected.

The infrared spectra of the resulting diketones contained only the deformation frequencies corresponding to the $-\text{CH}=\text{CH}-$ grouping (about 968 cm^{-1}); the vinyl group frequencies were absent.

In the case of the telomer of 1,3-butadiene with piperylene hydrochloride, we made use of a mixture of the allylic isomers, but the telomer with a terminal vinyl group did not enter into reaction under the experimental conditions.

An experiment with 1,3-dichloro-5-methyloctadiene (in a medium of anhydrous alcohol [3]) did not give the expected diketone but the product of its hydrolytic cleavage—6-chloro-4-methyl-2,6-undecadien-10-one. The latter was identical with the product of hydrolysis of the corresponding alkadienylacetoacetic ester which we described earlier [1].

The prepared diketones are colorless liquids with a characteristic odor, insoluble in water. Their constants are set forth in the table. We see from the table that the molecular refractions found for the diketones are considerably higher than the calculated values in each case. Common to all the infrared spectra (see figure) are the strong carbonyl group bands in the $1705\text{--}1725\text{ cm}^{-1}$ region, bands around 1160 cm^{-1} which are characteristic of methylketones, and the strong bands at about 1360 cm^{-1} which are also



Infrared transmission spectra. 1) 3-[5-methyl-2,6-octadienyl]-2,4-pentanedione; 2) 3-chloro-5-methyl-2,6-octadienyl-2,4-pentanedione; 3) 3-[3,5-dimethyl-2,6-octadienyl]-2,4-pentanedione.

usually present in ketones. The double bond is associated with the frequency of about 1605 cm^{-1} which is lower than the normal value.

Constants and Analytical Data for Products of Condensation

Substance	B.p. (5 mm)	d_4^{20}	n_D^{20}	MR	
				found	calc.
(I) $\text{CH}_3-\text{CH}=\text{CH}-\underset{\text{CH}_3}{\text{CH}}-\text{CH}_2-\text{CH}=\text{CH}-\underset{\text{CO}-\text{CH}_3}{\text{CH}}-\text{CO}-\text{CH}_3$	128–130°	0.9270	1.4770	67.60	65.84
(II) $\text{CH}_3-\text{CH}=\text{CH}-\underset{\text{CH}_3}{\text{CH}}-\text{CH}_2-\text{CCl}=\text{CH}-\underset{\text{CO}-\text{CH}_3}{\text{CH}}-\text{CO}-\text{CH}_3$	150–152	1.0230	1.4905	73.46	70.81
(III) $\text{CH}_3-\text{CH}=\text{CH}-\underset{\text{CH}_3}{\text{CH}}-\underset{\text{CH}_3}{\text{CH}}-\text{C}=\text{CH}-\underset{\text{CO}-\text{CH}_3}{\text{CH}}-\text{CO}-\text{CH}_3$	136–137	0.9283	1.4820	72.56	70.56

All of the isolated substances give qualitative reactions with TiCl_3 , o-phenylenediamine, and $\text{Cu}(\text{OCOCH}_3)_2$ which are characteristic of β -diketones [4]. Crystalline 2,4-dinitrophenylhydrazones could only be prepared from two of the diketones (II) and (III).

Heating of diketone (II) with urea in presence of HCl led to three crystalline condensation products whose structure we did not establish.

EXPERIMENTAL

A mixture comprising 20 g of sodium acetylacetonate [5], the equivalent quantity of telomer, and 200 ml of anhydrous acetone, was heated on a water bath at the boil for 50–60 hr with mechanical stirring. It was then diluted with double the volume of water. The reaction products were extracted from the aqueous layer with ether. The ethereal extract, combined with the upper layer, was dried over calcined MgSi_4 . After the ether had been taken off, the residue was fractionated in vacuo in a Widmer column. Yield of diketones 20–25 %. Analytical data are set forth in the table.

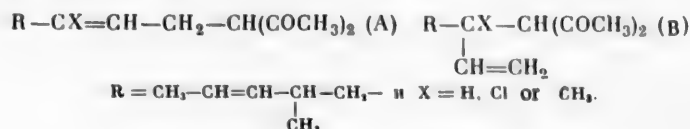
The infrared spectra were taken with the IKS-14 spectrophotometer using a NaCl prism. Layer thickness 32 μ .

Melting points and analytical data for the bis-2,4-dinitrophenylhydrazones are given in the table.

A mixture of 1.3 g of diketone (II), 0.5 g of urea, 0.8 ml of conc. HCl, and 40 ml of alcohol was heated on a water bath at the boil for 10 hr. After the mixture had cooled, it was diluted with ether; colorless crystals came down. These were separated into three portions by recrystallization from water: 1) m.p. 176–178° (with decomp.), insoluble in water, nitrogen content 12.92%; 2) m.p. 176–176.5°, soluble in water with a yellow color, nitrogen content 9.22%; 3) m.p. 119°, soluble in water, nitrogen content 8.21%.

SUMMARY

1. The reaction with sodium acetylacetonate of the primary products of telomerization of 1,3-butadiene, chloroprene, and isoprene with piperylene hydrochloride was investigated.
2. A diketone was isolated in each case. Crystalline 2,4-dinitrophenylhydrazones of two of them were obtained.
3. It was shown that the exchange reaction goes as in other cases with formation of products of the crotyl type.



Found, %			Empirical formula	Calculated, %			Bis-2,4-dinitrophenylhydrazones			
C	H	Cl		C	H	Cl	melting point	found % N	Empirical formula	Calc. % N
74.34, 74.64	9.85, 10.00	—	$C_{14}H_{22}O_2$	75.63	9.97	—	—	—	—	—
65.66, 65.68	8.49, 8.49	13.84, 14.03	$C_{14}H_{21}O_2Cl$	65.49	8.24	13.81	68—70°	18.27, 18.32	$C_{26}H_{20}O_8N_8Cl$	18.16
76.17, 76.29	10.20, 10.29	—	$C_{15}H_{24}O_2$	76.25	10.29	—	58—60	19.13	$C_{27}H_{32}O_8N_8$	19.10

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INVESTIGATIONS ON DIPYRRYLMETHENES

III. SYNTHESIS OF MESO-SUBSTITUTED DIPYRRYLMETHENES

E. I. Filippovich, R. P. Evstigneeva, and N. A. Preobrazhenskii

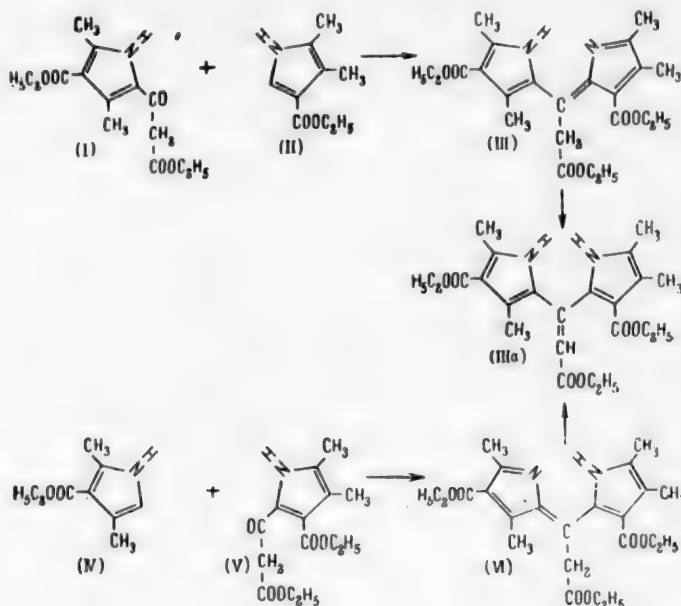
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Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

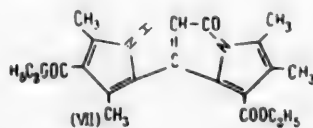
pp. 2968-2972, September, 1961

Original article submitted June 4, 1960

In continuation of our work on the synthesis of dipyrromethanes, we have now prepared 3,5,4',5'-tetramethyl-4,3'-dicarboxymesocarbethoxymethyl-dipyrromethene (III) by condensation of the ethyl ester of β -(2,4-dimethyl-3-carbethoxy-5-pyrrolyl)- β -ketopropionic acid (I) with 2,3-dimethyl-4-carbethoxypyrrole (II).

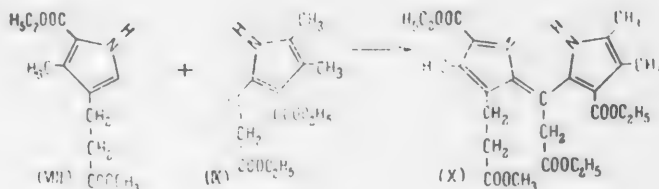


We isolated two forms of this compound: the methene form (III) with m.p. 118-120° and a violet color, and the ethylenic form (IIIa) with m.p. 192-193.5° and a yellow color. The latter was identical in properties with the ethylenic form of 4,5,3',5'-tetramethyl-3,4'-dicarboxy-mesocarbethoxymethyldipyrromethene (VI), m.p. 184-185.5°, prepared earlier by condensation of the ethyl ester of β -(2,3-dimethyl-4-carbethoxy-5-pyrrolyl)- β -keto-propionic acid (V) with 2,4-dimethyl-3-carbethoxypyrrole (IV) [1]. Both compounds [the yellow, ethylenic form (IIIa) with m.p. 192-193.5° from compound (III), and the yellow, ethylenic form (IIIa) with m.p. 184-184.5° from compound (VI)] have identical ultraviolet and infrared absorption spectra [2] and do not give a melting point depression (a mixed specimen melts at 190-193°). The difference in melting point is evidently due to rotational stereo-isomerism. Transition of the methene form of compound (III) into the ethylenic form [the base (IIIa)] is also accompanied by formation of the lactam (VII).



In the present work we also succeeded in isolating the methene form of 4,5,3',5'-tetramethyl-3,4'-dicarbethoxy-mesocarbethoxymethyl-dipyrlylmethene (VI) in spite of the difficulties associated with the facility of its transition to the ethylenic form. Compounds (III) and (VI) differ only in the position of the double bond, and due to prototropic rearrangement they give the same ethylenic form. Transition from compound (III) to (VI) is possible via the ethylenic form [2]. These results are very important in connection with the synthesis of porphyrinic systems.

The method that we developed for preparation of meso-substituted dipyrlylmethenes was successfully applied to the synthesis of 4,5,4'-trimethyl-3,5'-dicarbethoxy-3'-(ω -carbomethoxyethyl)-mesocarbethoxymethyl-dipyrlylmethene (X) from the methyl ester of β -(4-methyl-5-carbethoxy-3-pyrlyl)-propionic acid (VIII) and the ethyl ester of β -(2,3-dimethyl-4-carbethoxy-5-pyrlyl)- β -ketopropionic acid (IX). Compound (X) can be used in the synthesis of chlorophyll and related porphyrins.



EXPERIMENTAL

3,5,4',5'-Tetramethyl-4,3'-dicarbethoxy-mesocarbethoxymethyldipyrlylmethene (III). A solution of 0.37 g of the ethyl ester of β -(2,4-dimethyl-3-carbethoxy-5-pyrlyl)- β -ketopropionic acid (I) and 0.22 g of 2,3-dimethyl-4-carbethoxypyrrole (II) was prepared in 15 ml of anhydrous chloroform, and 0.76 g of phosphorus pentoxide was added in small portions with vigorous stirring. The mixture was held for 4 hr at 60°. The chloroform was decanted, washed with water until neutral, and distilled off in vacuo. The residue was triturated repeatedly with ligroine until a colorless filtrate was obtained. The preparation was purified by reprecipitation from ether with ligroine. An amorphous, violet-red substance with m.p. 118-120°. Yield 0.11 g (19.4 %).

λ_{\max} 300 m μ (log ϵ 4.2), 410 m μ (log ϵ 3.9), 592 m μ (log ϵ 3.4).

Found %: C 64.37; H 7.12; N 6.64. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.15; H 7.03; N 6.50.

4,5,3',5'-Tetramethyl-3,4'-dicarbethoxy-mesocarbethoxymethyldipyrlylmethene (IIIa). A solution of 0.57 g of 2,3-dimethyl-4-carbethoxypyrrole (II) and 0.96 g of the ethyl ester of β -(2,4-dimethyl-3-carbethoxy-5-pyrlyl)- β -ketopropionic acid (I) was prepared in 20 ml of anhydrous chloroform and with vigorous stirring 2 g of phosphorus pentoxide was added in small portions. The mass was then heated for 4 hr at 55-60°. After the reaction mass had cooled, 30 ml of 1% ammonia solution was added. The chloroform layer was separated and washed with water until neutral. The solvent was removed in vacuo. The residual oil was repeatedly triturated with ligroine. The insoluble residue was recrystallized from alcohol and the light-yellow product was dried in a vacuum-desiccator. Yield 0.16 g (14.65%). M.p. 192-194.5°.

λ_{\max} 350 m μ (log ϵ 4.3).

Found %: C 64.49; H 6.80; N 6.64. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.15; H 7.03; N 6.50.

Lactam of 3,5,4',5'-tetramethyl-4,3'-dicarbethoxy-mesocarbomethyldipyrlylmethene (VII). A solution of 0.57 g of 2,3-dimethyl-4-carbethoxypyrrole (II) and 0.96 g of the ethyl ester of β -(2,4-dimethyl-3-carbethoxy-5-pyrlyl)- β -ketopropionic acid (I) was prepared in 20 ml of anhydrous chloroform, and 2 g of phosphorus pentoxide was added portionwise with vigorous stirring. The mixture was then heated at 55-60° for 4 hr. After the reaction mass had cooled, 30 ml of 10% ammonia solution was added. The chloroform layer was separated and washed with water until neutral. The solvent was taken off in vacuo. The product was extracted from the residue with ligroine, the solvent removed in vacuo, and the residue treated with 5 ml of alcohol. The precipitate was collected and recrystallized from alcohol. Bright-yellow crystals, M.p. 238-240°.

λ_{\max} 430 m μ (log ϵ 3.8).

Found %: C 65.89; H 6.13; N 7.44. $C_{21}H_{24}O_5N_2$. Calculated %: C 65.60; H 6.29; N 7.29.

4,5,3',5'-Tetramethyl-3,4'-dicarbethoxy-mesocarbethoxymethyldipyrrolylmethene (VI). To a solution of 0.37 g of ethyl ester of β -(2,3-dimethyl-4-carbethoxy-5-pyrrolyl)- β -ketopropionic acid (V) and 0.22 g of 2,4-dimethyl-3-carbethoxypyrrole (IV) in 15 ml of anhydrous chloroform was added in small portions 0.76 g of phosphorus pentoxide. The reaction mass was stirred for 4 hr at 60°. The chloroform was decanted and washed with water until neutral. After the solvent had been taken off in vacuo, the residue was repeatedly triturated with ligroine until a colorless filtrate was obtained. The residue was purified by reprecipitation from ether with ligroine. An amorphous, violet substance was obtained and was dried in a vacuum-desiccator. Yield 0.17 g (30%). M.p. 147-148°.

λ_{\max} 410 m μ (log ϵ 3.9), 505 m μ (log ϵ 3.6), 584 m μ (log ϵ 3.7), 685 m μ (log ϵ 3.3).

Found %: C 64.10; H 6.91; N 6.53. $C_{23}H_{30}O_6N_2$. Calculated %: C 64.15; H 7.03; N 6.50.

Methyl ester of β -(2-carboxy-4-methyl-5-carbethoxypyrrolyl)-propionic acid. Dropwise addition of 21.5 g of sulfonyl chloride was made, with stirring at a temperature not higher than 4°, to a solution of 13.28 g of methyl ester of β -(2,4-dimethyl-5-carbethoxy-3-pyrrolyl)-propionic acid in 55 ml of absolute ether. The reaction mass was then held at below 0° for an hour and at 18-20° for 3 hr. The ether was removed in vacuo. A boiling solution of sodium acetate (44.5 g in 720 ml of water) was run into the residue and the mass was heated with vigorous stirring for 5 min. The ice-cooled solution deposited a precipitate which was filtered, washed with water (twice with 50 ml each time), and dissolved in 300 ml of saturated sodium bicarbonate solution. The solution of the sodium salt was saturated with sulfur dioxide at room temperature until it had a weakly acid reaction (to Congo). The white precipitate was collected, washed with water (four lots of 25 ml each), and thoroughly pressed on a filter. The product was recrystallized from methanol and dried in a vacuum-desiccator. Yield 10.19 g (68.2%). M.p. 175-176°.

Found %: C 55.16; H 6.09; N 5.23. $C_{17}H_{17}O_6N$. Calculated %: C 55.11; H 6.05; N 4.95.

Methyl ester of β -(4-methyl-5-carbethoxy-3-pyrrolyl)-propionic acid (VIII). The methyl ester of β -(2-carboxy-4-methyl-5-carbethoxy-3-pyrrolyl)-propionic acid (1 g) was placed in a Claisen flask and heated for an hour at 230-240° in a nitrogen stream. The residue was distilled in vacuo. B.p. 136-138° (7 mm). Yield 0.66 g (78.5%). A colorless, crystalline substance. M.p. 47-48°.

Found %: C 60.70; H 7.47; N 5.84. $C_{17}H_{17}O_4N$. Calculated %: C 60.24; H 7.16; N 5.85.

4,5,4'-Trimethyl-3,5'-dicarbethoxy-3'-(ω -carbomethoxyethyl)-mesocarbethoxymethyldipyrrolylmethene (X). To a solution of 0.5 g of methyl ester of β -(4-methyl-5-carbethoxy-3-pyrrolyl)-propionic acid and 0.59 g of ethyl ester of β -(2,3-dimethyl-4-carbethoxy-5-pyrrolyl)- β -ketopropionic acid in 20 ml of anhydrous chloroform was added 1 g of phosphorus pentoxide in small portions. The mixture was stirred at 60° for 4 hr. To the reaction mixture was then added 50 ml of 1% ammonia solution. The chloroform layer was separated and washed with water until neutral (five lots of 30 ml each). The chloroform was removed in vacuo. The residue was washed with gasoline (four lots of 25 ml each) and purified by reprecipitation from ether with ligroine. An amorphous, brown substance. Yield 0.23 g (25.7%). M.p. 138-140°.

λ_{\max} 415 m μ .

Found %: C 62.23; H 6.38; N 5.42. $C_{26}H_{34}O_8N_2$. Calculated %: C 62.15; H 6.82; N 5.57.

SUMMARY

1. A series of dipyrrolymethenes with a carbethoxymethyl substituent in the meso-position was synthesized: 3,5,4',5'-tetramethyl-4,3'-dicarbethoxy-mesocarbethoxymethyldipyrrolylmethene; 4,5,3',5'-tetramethyl-3,4'-dicarbethoxy-mesocarbethoxymethyldipyrrolylmethene; lactam of 3,5,4',5'-tetramethyl-4,3'-dicarbethoxy-mesocarbethoxymethyldipyrrolylmethene; 4,5,4'-trimethyl-3,5'-dicarbethoxy-3'-(ω -carbomethoxyethyl)-mesocarbethoxymethyldipyrrolylmethene.

2. The methene and ethylenic forms of the first two compounds were isolated.

3. A method was developed for preparation of the methyl ester of β -(2-carboxy-4-methyl-5-carbethoxy-3-pyrrolyl)-propionic acid and the methyl ester of β -(4-methyl-5-carbethoxy-3-pyrrolyl)-propionic acid.

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STUDIES IN THE DIPYRRYLMETHENE SERIES

IV. SYNTHESIS OF UNSYMMETRICAL DIPYRRYLMETHENES

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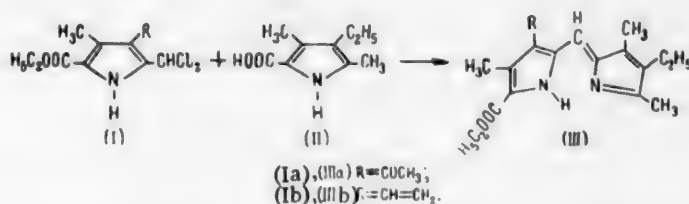
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pp. 2972-2975, September, 1961

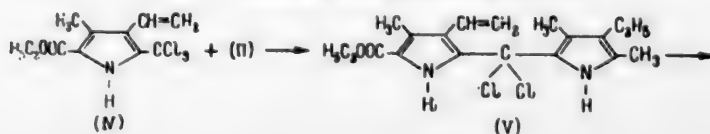
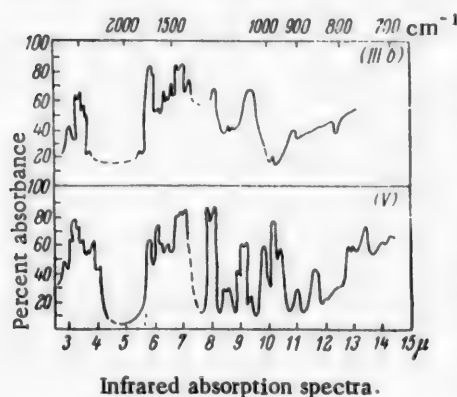
Original article submitted June 15, 1960

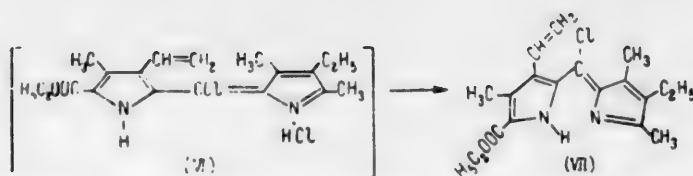
The currently known syntheses of porphyrins are based on dipyrromethenes. However, the unsymmetrical dipyrromethenes, which could be used to obtain porphyrins related to chlorophyll, are still difficultly available. The most efficient procedure is the aldehyde synthesis, although in a large number of cases even this method is complicated by the obtaining of symmetrical dipyrromethenes [1-3]. In this connection a study of new paths for the synthesis of unsymmetrical dipyrromethenes possesses considerable interest. In this paper we report on the synthesis of unsymmetrical dipyrromethenes, starting with the dichloromethyl derivatives of pyrrole. The latter are intermediate products in the preparation of aldehydes from the corresponding methylpyrroles.

2-Dichloromethyl-3-acetyl-4-methyl-5-carbethoxypyrrole [4] (Ia, R = COCH₃) when reacted with 2,4-dimethyl-3-ethylpyrrole-5-carboxylic acid [5, 6] (II) gives the hydrochloride of 4,3',5'-trimethyl-3-acetyl-4'-ethyl-5-carbethoxydipyrromethene (IIIa, HCl).



The presence in compound (Ia) of the electron-acceptor acetyl group in the 3 position of the pyrrole ring inhibits the reaction to a large degree, and to make the reaction go requires an acid catalyst and heating. The presence of the electron-donor vinyl group in the 3 position, as is the case in 2-chloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole (Ib), leads to exceedingly easy reaction with 2,4-dimethyl-3-ethylpyrrole-5-carboxylic acid (II), which takes place on simple mixing of the reactants in methyl alcohol, giving 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxydipyrromethene (IIIb). An analogous reaction also takes place with the trichloro derivatives (IV). In this case the reaction goes via the formation of the dichlorodipyrromethane (V), which cleaves one of the chlorine atoms with exceeding ease to yield the hydrochloride of the meso-chloro dipyrromethene derivative (VI). The free base of the meso-chloro dipyrromethene derivative (VII) is isolated from the hydrochloride by treatment of the latter with alkaline agents, or it is obtained from the dichlorodipyrromethane (V) under the same conditions. This reaction was observed by us to be a secondary reaction in the preparation of the dipyrromethene from technical 3-vinyl-4-methyl-2-dichloromethylpyrrole, which contains a small amount of the trichloro derivative.





The structure of the obtained compounds was confirmed by the infrared spectra (figure), where the absorption bands of all of the characteristic groups were found to be present.

EXPERIMENTAL

Hydrochloride of 4,3',5'-trimethyl-3-acetyl-4'-ethyl-5-carbethoxydipyrromethene (IIIa, HCl, R = COCH₃). One gram of 2-dichloromethyl-3-acetyl-4-methyl-5-carbethoxypyrrole (m.p. 157.5-158°) [4] was rubbed with 0.64 g of 2,4-dimethyl-3-ethyl-5-carboxylic acid. Then 2 ml of anhydrous methanol was added, followed by the addition of 2 ml of cooled to 0° hydrobromic acid. The reaction mass was heated at 60° for 30 min. After cooling to 0°, the precipitate was filtered and reprecipitated from glacial acetic acid solution with ether. The compound was obtained as slightly yellow crystals. M.p. 248-250° (rapid heating).

Found %: C 62.83; H 7.10; N 7.97. C₁₉H₂₅O₃N₂Cl. Calculated %: C 62.53; H 6.91; N 7.68.

Free base 4,3',5'-trimethyl-3-acetyl-4'-ethyl-5-carbethoxydipyrromethene (IIIa, R = COCH₃). A solution of 0.3 g of the hydrochloride of 4,3',5'-trimethyl-3-acetyl-4'-ethyl-5-carbethoxydipyrromethene in 150 ml of water was treated with 3 ml of 10% ammonia. The precipitated base was extracted with chloroform. Then the solvent was distilled off and the residue was triturated with anhydrous ether, followed by reprecipitation from alcohol solution with ether. A brown amorphous substance was obtained. M.p. 209-210° (with decomp.) [7].

Found %: N 8.67. C₁₉H₂₄O₃N₂. Calculated %: N 8.53.

2-Dichloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole (Ib, R = CH = CH₂). With external cooling in ice and constant shaking, a solution added dropwise to a solution of 1.1 g of 2-methyl-3-vinyl-4-methyl-5-carbethoxypyrrole [4] (m.p. 111-112°) in 65 ml of absolute ether. The reaction mass was allowed to stand at 0-3° for 7 hr, after which it was washed with 30 ml of saturated sodium bicarbonate solution, cooled to -2 to -4°. The ether extract was dried over sodium sulfate. The solvent was removed by distillation. The crystalline residue was washed with a little absolute ether. Yield 1.42 g (94%). After recrystallization from ether, m.p. 154-155°. Colorless crystals, readily soluble in the common organic solvents.

Found %: C 50.70; H 5.29; N 5.24; Cl 27.01. C₁₁H₁₃O₂NCl₂. Calculated %: C 50.40; H 4.99; N 5.34; Cl 27.05.

4,3',5'-Trimethyl-3-vinyl-4'-ethyl-5-carbethoxydipyrromethene (IIb, R = CH = CH₂). 2-Dichloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole (0.52 g) was rubbed with 0.38 g of 2,4-dimethyl-3-ethylpyrrole-5-carboxylic acid, followed by the addition of 1.3 ml of anhydrous methyl alcohol. Here the precipitate dissolved completely, and the evolution of carbon dioxide was observed. The reaction mass was allowed to stand at 2-4° for 10 to 12 hr. The solvent was removed by distillation. The residue was triturated with dry ether. This resulted in the deposition of a greenish-brown precipitate. M.p. 170-172°. Yield 0.8 g. The technical hydrochloride was dissolved in 150 ml of water and the solution was neutralized with potassium carbonate. The yellow oil that separated here was extracted with ether. The extract was dried over potassium carbonate. The solvent was removed by distillation. The residue, a light-colored yellow-brown powder, was recrystallized from petroleum ether. Yield 0.40 g (61.8%). M.p. 115-117°.

Found %: C 73.00; H 7.48; N 8.88. C₁₉H₂₄O₂N₂. Calculated %: C 73.05; H 7.74; N 8.96.

4,3',5'-Trimethyl-3-vinyl-4'-ethyl-5-carbethoxy-meso-dichlorodipyrromethane (V). Technical 2-dichloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole (1.65 g), containing a small amount of 2-trichloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole, was rubbed with 1.2 g of 2,4-dimethyl-3-ethylpyrrole-5-carboxylic acid, followed by the addition of 4 ml of anhydrous methanol to the mixture. A crystalline precipitate deposited after standing for a short while. The reaction mass was allowed to stand at 1-3° for 10 to 12 hr. The precipitate was filtered and washed with 2 ml of alcohol. We obtained 0.3 g of bright orange-red crystals, readily soluble in benzene and ether, and difficultly soluble in water and alcohol. M.p. 172-174° (rapid heating). Recrystallization of the obtained compound (V) from alcohol proved unsuccessful.

Found %: C 60.02; H 6.15; N 7.13; Cl 18.20. C₁₉H₂₄O₂N₂Cl₂. Calculated %: C 59.54; H 6.31; N 7.31; Cl 18.50.

The solvent was removed from the mother liquor by distillation, and the residue was worked up as described above to give 1.9 g of the hydrochloride of 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxydipyrromethene (IIb, $R = CH = CH_2$). M.p. 170-172°.

4,3',5'-Trimethyl-3-vinyl-4'-ethyl-5-carbethoxy-meso-chlorodipyrromethene (VII). A solution of 0.15 g of 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxy-meso-dichlorodipyrromethane in 40 ml of benzene was washed with saturated potassium carbonate solution. The extract was dried over potassium carbonate. Then the solvent was removed by distillation and the residue was triturated with a small amount of alcohol. This resulted in the deposition of bright red crystals, readily soluble in ether and in petroleum ether. M.p. 108-109°.

Found %: N 7.77; Cl 10.2. $C_{19}H_{23}O_2N_2Cl$. Calculated %: N 8.05; Cl 10.23.

SUMMARY

1. 4,3',5'-Trimethyl-3-acetyl-4'-ethyl-5-carbethoxydipyrromethene and 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxydipyrromethene were synthesized.
2. In the course of the synthesis, along with the principal products – the unsymmetrical dipyrromethenes – we also isolated and characterized the compounds 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxy-meso-dichlorodipyrromethane and 4,3',5'-trimethyl-3-vinyl-4'-ethyl-5-carbethoxy-meso-chlorodipyrromethene.
3. A method was developed for obtaining 2-dichloromethyl-3-vinyl-4-methyl-5-carbethoxypyrrole.
4. It was shown that the reactivity of the dichloromethyl group in the starting pyrrole derivative is mainly dependent on the character of the substituent in the 3 position of the pyrrole ring. The corresponding trichloromethyl derivatives can serve as a source for obtaining the unsymmetrical meso-chloro dipyrromethene derivatives.

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STUDIES IN THE DIPYRRYLMETHENE SERIES

V. INFRARED ABSORPTION SPECTRA OF MESO-SUBSTITUTED

DIPYRRYLMETHENES

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To construct the porphyrin molecule of chlorophyll it is necessary to have two dipyrromethenes. One of them should have a substituent in the meso-position, which at a certain stage in the synthesis can be converted to the chloropentanone group, present in chlorophyll. The infrared spectra of the dipyrromethenes have received little study, although they can furnish very valuable information for establishing the structure of these compounds.

We made a study of the infrared absorption spectra of a group of dipyrromethenes having a substituent in the meso-position [1, 2], the synthesis of which was based on the following four pyrrole derivatives: ethyl ester of β -(2,4-dimethyl-3-carbethoxy-5-pyrrolyl)- β -ketopropionic acid (I); 2,4-dimethyl-3-carbethoxypyrrole (II); ethyl ester of β -(2,3-dimethyl-4-carbethoxy-5-pyrrolyl)- β -ketopropionic acid (III); and 2,3-dimethyl-4-carbethoxypyrrole (IV).

As a result of the combination in pairs of compounds (I) and (III) with (II) and (IV) we obtained four dipyrromethenes which differ from each other only in the variations of the same substituents in the β -position.

The starting compounds (I)-(IV) in the crystalline state (molded with KBr into disks) show strong absorption in the region of the NH stretching vibrations, localized around 3300 cm^{-1} (Fig. 1). This is approximately 150 cm^{-1} lower than the value ($3440\text{--}3480\text{ cm}^{-1}$) found for the absorption of the free NH group in substituted pyrroles [3].

The shift in the long-wave region and, in addition, the sharp outline of the absorption both suggest that compounds (I)-(IV) exhibit intermolecular association in the solid state.

One strong band around 1670 cm^{-1} appears in the region of the stretching vibrations of the C = O bond in compounds (II) and (IV) (Fig. 1); the marked reduction in this value when compared with the normal value of $1735\text{--}1750\text{ cm}^{-1}$ for ester groups is due to conjugation with the pyrrole ring. Compounds (I) and (III) exhibit three types of absorption by the C = O group: in addition to the above mentioned carbethoxyl group, conjugated with the ring, which exhibits absorption here at 1690 cm^{-1} (I) and 1720 cm^{-1} (III), there are two other bands: 1730 cm^{-1} (I) and 1740 cm^{-1} (III) (isolated carbethoxy group), and 1625 cm^{-1} (I) and 1630 cm^{-1} (III) (keto group, conjugated with the ring) (Fig. 1).

Based on compounds (I)-(IV), an interesting relationship appears between the position of the methyl substituents in the pyrrole ring and the activity of the stretching vibrations of the ring in the spectrum. Compounds (III) and (IV), each having methyl groups in the 2,3-positions, give one band in the vicinity of 1500 cm^{-1} , corresponding to the symmetrical vibrations of the ring, whereas compounds (I) and (II) exhibit, in addition to this band, also a distinct band at 1560 cm^{-1} (I) and 1580 cm^{-1} (II), which can be attributed to the antisymmetrical stretching vibrations of the pyrrole ring. A similar dependence of the activity of the stretching vibrations of the pyrrole ring on the position of the substituents in the ring was also observed by other authors for the case of the 2,4- and 2,5-disubstituted pyrroles [4]. The first of the two bands, 1565 and 1500 cm^{-1} , attributed to the stretching vibrations of the ring, proved to be more intense in the case of the 2,4-disubstituted pyrroles and less intense in the case of 2,5-substitution.

In the region of the NH stretching vibrations, the symmetrically substituted dipyrromethene (V) fails to show as clearly defined absorption as the starting pyrroles (I) and (II). Together with this, a highly diffuse broad band appears in the solid state, having a peak located between $3200\text{--}3250\text{ cm}^{-1}$ [(V), KBr, see Fig. 1]. The intramolecular

character of the association, which is suggested by the shape and position of the band, is confirmed by the spectrum of the dilute solution of the compound in chloroform, where the picture of the absorption in the NH region hardly changes, and where a distinct band fails to appear in the range $3440\text{--}3480\text{ cm}^{-1}$, characteristic for the free NH group of pyrroles in solution [(V), CHCl_3 , see Fig. 1].

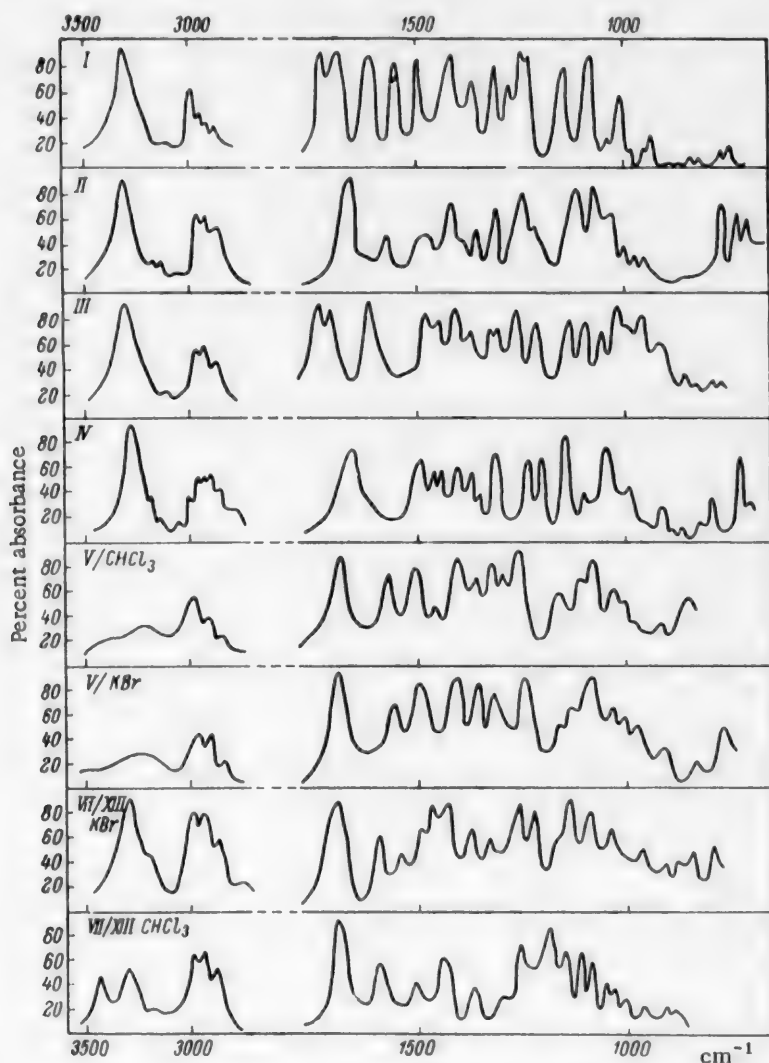
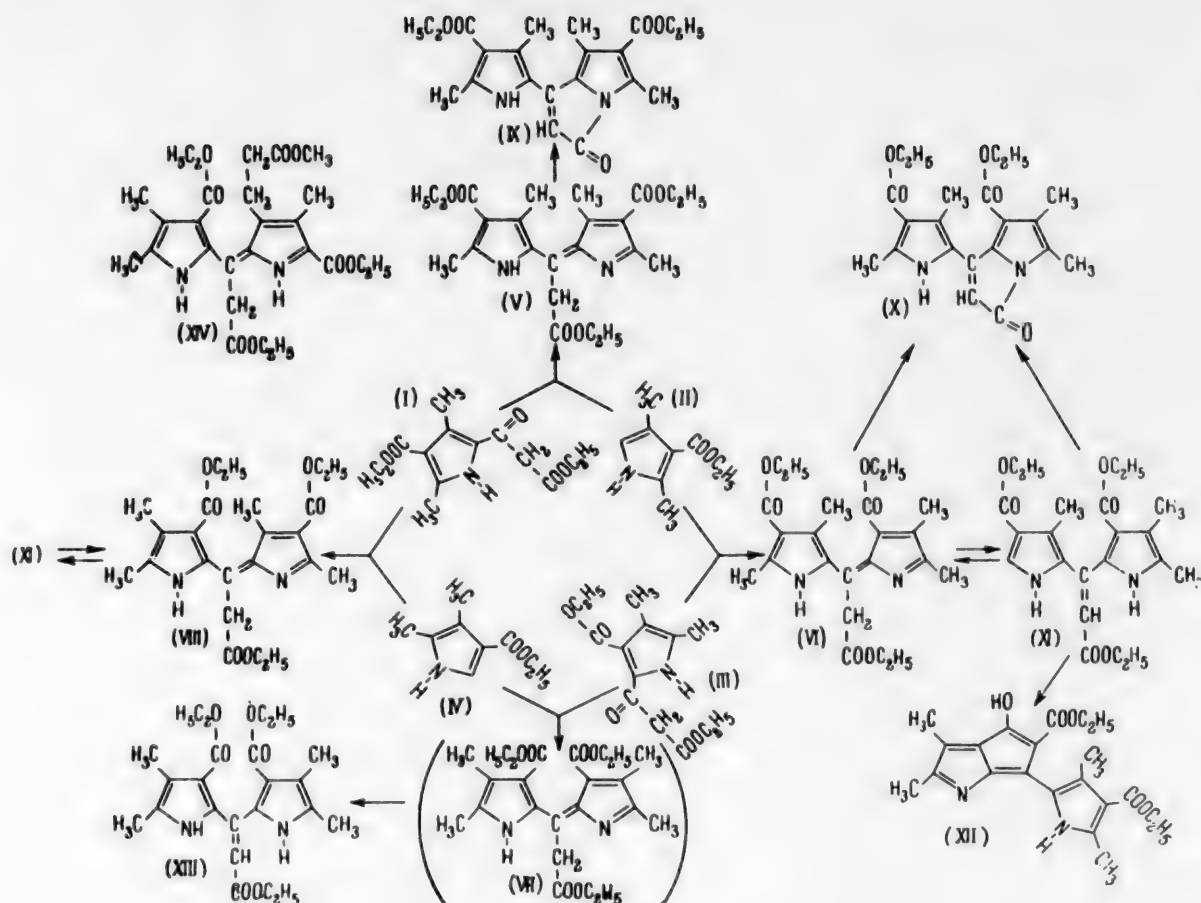


Fig. 1. Infrared absorption spectra. I-IV, V, VII/XIII) Molded into disks with KBr at 150 atm, in a vacuum of 0.1 mm. V and VII/VIII) 0.2 M solution in CHCl_3 , layer thickness 0.050 mm.

A single band at 1700 cm^{-1} appears in the region of the absorption of the $\text{C}=\text{O}$ group, corresponding to the carbethoxyl group, conjugated with the ring. The absence of absorption some $20\text{--}30\text{ cm}^{-1}$ above this value, which could be expected in view of the presence of the isolated carbethoxy group of the meso-substituent, is additional proof of the presence of intramolecular association, accomplished between the NH and the $\text{C}=\text{O}$ group of the meso-substituents, and causing a decrease in the frequency of the latter to a value coinciding with the absorption of the carbethoxyl groups in the ring.

Both of the vibration frequencies of the pyrrole ring, mentioned above for compounds (I) and (II), also prove to be present in the infrared spectrum of compound (V), namely, at 1515 and 1570 cm^{-1} , in accordance with the 2,4-position of the methyl groups in the two rings.



Another symmetrically substituted dipyrromethene, obtained from pyrroles (III) and (IV), does not exist in the free state, as has been shown by us previously [5], in the form of (VII), but instead it undergoes prototropic, the so-called "methene-ethylene," rearrangement, converting to form (XIII). Its spectrum in the NH region exhibits a strong, sharp band at 3330 cm^{-1} [(VII/XIII), KBr, see Fig. 1], analogous to the absorption shown in this region by the starting pyrroles (III) and (IV). In chloroform solution this band splits into two bands, in which connection the absorption at 3300 cm^{-1} is reduced somewhat in intensity [(VII/XIII), CHCl_3 , see Fig. 1] (that the frequency is reduced can be judged by comparing with the absorption value of the CH bonds in the neighboring $2800\text{--}3000\text{ cm}^{-1}$ region) and a sharp peak appears at 3440 cm^{-1} , corresponding to the free NH group. The described behavior is explained by the presence of intermolecular association, which in solution is destroyed on dilution.

Absorption in the $\text{C}=\text{O}$ region consists of one band at 1690 cm^{-1} ; in this case an equalization of the frequencies of the carbethoxy groups in the ring and in the side chain is due to conjugation of the latter through the ethylene bond with the entire system.

Intense absorption at 1600 cm^{-1} is most naturally attributed to the stretching vibrations of the ethylene bond, since the value of this vibration is slightly high for the vibrations of the pyrrole ring, if it is considered that for pyrrole itself the highest vibration frequency of its ring is equal to 1575 cm^{-1} [6].

The weak band at 1510 cm^{-1} , detected in chloroform solution [(VII/XIII), CHCl_3 , see Fig. 1], is attributed to the vibrations of the ring; in this connection the absence of a second band in the vicinity of 1550 cm^{-1} is in harmony with the statement made above regarding the influence of the position of the methyl groups on the activity of the vibrations of the ring in the infrared spectrum, since in the present case we are dealing with the 2,3-position. For

compound (XIII) weak absorption at 1560 cm^{-1} appears only in the solid state [(VII/XIII), KBr, see Fig. 1], apparently, caused by the influence of the intermolecular forces of the crystal lattice.

In addition to the two symmetrical dipyrromethenes discussed above, two unsymmetrical dipyrromethenes (VI) and (VIII) are also obtained from a coupling in pairs of the starting pyrroles (I) and (IV), and (II) and (III). These two compounds behave differently in the region of NH absorption. Here dipyrromethene (VI) in the solid state exhibits a strong, distinct band at 3305 cm^{-1} [(VI), KBr, see Fig. 2], whereas dipyrromethene (VIII) fails to show well-defined absorption, represented here by a highly diffuse band with a center at approximately $3200\text{--}3250\text{ cm}^{-1}$ [(VIII), KBr, see Fig. 2]. When dissolved in chloroform, compound (VI) exhibits a new sharp band at 3440 cm^{-1} , which, similar to the 3440 cm^{-1} frequency of the above discussed compound (XIII), relates to the vibrations of the free NH group, in which connection the intensity of the band at 3305 cm^{-1} shows a corresponding decrease [(VI), CHCl_3 , see Fig. 2], while in the case of compound (VIII) when dissolved in CHCl_3 there is no absorption in the region of the free NH group, with retention of a diffuse band at $3250\text{--}3200\text{ cm}^{-1}$ [(VIII), CHCl_3 , see Fig. 2].

The presented facts serve as evidence that the NH group in compound (VIII) is found in the state of intramolecular association, while in compound (VI) it is found in the state of intermolecular association. By analogy with compound (V), in the first case an intramolecular hydrogen bond is apparently formed between the hydrogen of the NH group and the oxygen of the ester group of the meso-substituent.

In the region of the $\text{C}=\text{O}$ stretching vibrations, compounds (VIII) and (VI) do not show any differences in absorption, exhibiting a strong band at 1710 cm^{-1} , both in solution and in the solid state.

Compounds (VI) and (VIII) exhibit several bands in the region from 1500 to 1650 cm^{-1} , variable in intensity depending on the aggregate state of the specimen. The bands below 1600 cm^{-1} : (VI) 1510 cm^{-1} in KBr, and 1525 cm^{-1} in chloroform—must be attributed, the same as in the previous cases, to the vibrations of the pyrrole ring.

Only compound (VI) exhibits distinct absorption above 1600 cm^{-1} , and specifically at 1625 cm^{-1} in KBr, which can be attributed to the bridging double bond. As was shown by us in a previous paper [5], dipyrromethenes (VI) and (VIII) can be converted via the "methene-ethylene" rearrangement to the same compound (XI). Here a characteristic dependence of the reactivity on the differences in the molecular structures of compounds (VI) and (VIII) is observed, being manifested in a different character of absorption in the NH region, and specifically: dipyrromethene (VI), where the above presented analysis of the spectra disclosed the presence of intermolecular association, undergoing destruction in solution, rearranges to the ethylene form (XI) much more easily than does dipyrromethene (VIII), where the analysis of the spectra revealed the presence of a strong intramolecular hydrogen bond.

Compound (XI), formed as the result of the rearrangement of compounds (VI) and (VIII), behaves in the region of NH absorption like a pyrrole derivative that exists only in the state of intermolecular association: in the solid state it exhibits a strong, sharp band at 3275 cm^{-1} , while in solution a distinct peak appears at 3440 cm^{-1} , with a corresponding reduction in the intensity of the band at 3275 cm^{-1} .

In the $\text{C}=\text{O}$ region, compound (XI) in chloroform solution exhibits a strong band at 1690 cm^{-1} , which in the solid state is split into two bands: 1680 and 1712 cm^{-1} [(XI), KBr and (XI), CHCl_3 , see Fig. 2]. A similar cleavage occurs with the single band of the stretching vibrations of the ring: from 1490 cm^{-1} to 1482 and 1515 cm^{-1} . The same as compound (XIII), (XI) also shows the presence of the ethylene bond in the infrared spectrum, exhibiting a fairly intense band at 1590 cm^{-1} in KBr, and at 1600 cm^{-1} in CHCl_3 .

The lactam (X) obtained from compound (XI) also absorbs in this region (1620 cm^{-1}), while in the region of the vibrations of the ring it displays two bands: a strong band at 1500 cm^{-1} and a weak band at 1550 cm^{-1} [(X), KBr, see Fig. 2]. Such an interrelationship in the intensities of these bands is understandable if we start with the following considerations. The frequency of the vibrations of the ring in the vicinity of 1500 cm^{-1} is present in the spectra of all of the examined substituted pyrroles, while the frequency around 1550 cm^{-1} is present mainly in the pyrroles having a 2,4-substitution of the methyl groups. Since in compound (X) one ring has a 2,4-substitution of the methyl groups, while the other ring has 2,3-substitution, then it is natural to expect that the band at 1500 cm^{-1} (to which the rings with both types of substitution contribute) will be at least twice as intense as the band at 1550 cm^{-1} . Additional proof that these same interrelationships of the spectra with the type of methyl substitution are retained in the dipyrromethenes is supplied by the spectrum of compound (XIV) in KBr (Fig. 2), where one has a 2,3-substitution of the methyl groups, while the other ring contains only a single methyl group. In accordance with expectation, the spectrum of compound (XIV) exhibits in the region of the vibrations of the ring a single intense band at 1500 cm^{-1} .

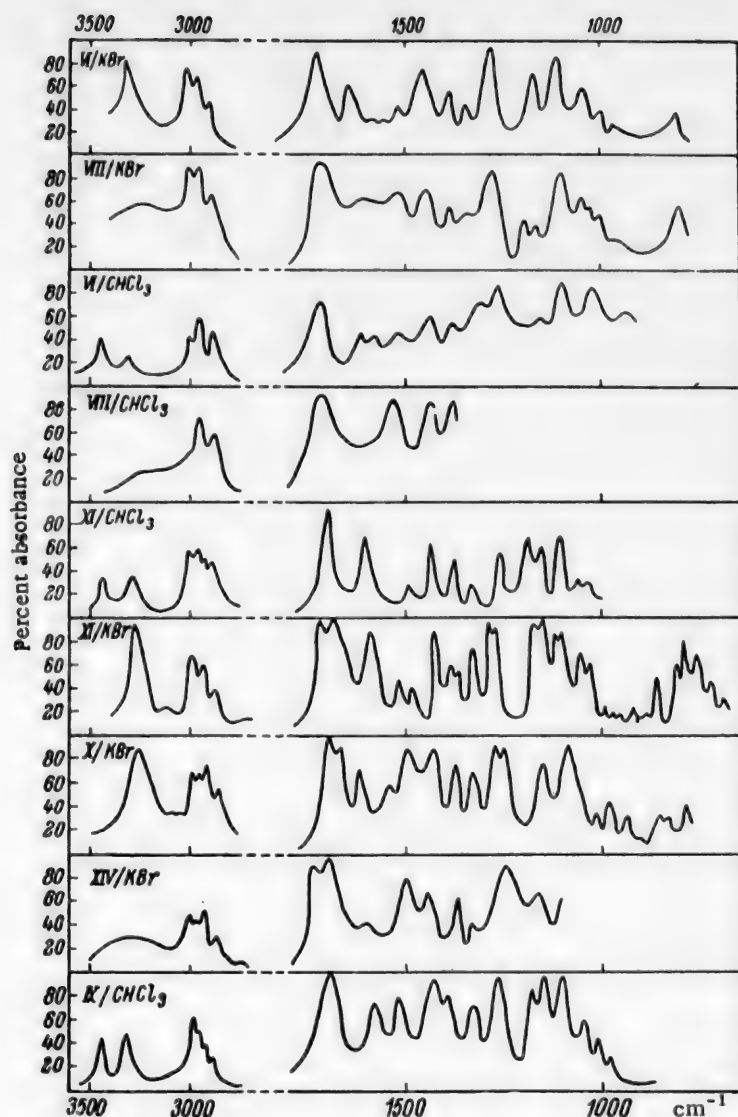


Fig. 2. Infrared absorption spectra. VI, VIII, X, XI and XIV) Molded into disks with KBr at 150 atm, in a vacuum of 0.1 mm. VI, VIII, IX and XI) 0.15 M solution in CHCl_3 , layer thickness 0.050 mm.

Lactam (IX), formed from the symmetrical dipyrromethene (V), also exists in the state of intermolecular association, displaying in chloroform solution two bands: at 3310 cm^{-1} (bound NH) and at 3440 cm^{-1} (free NH) [(IX), CHCl_3 , see Fig. 2]. All three of its C=O groups absorb at 1690 cm^{-1} , in contrast to lactam (X), where a cleavage of this band into 1700 and 1665 cm^{-1} is observed, in which connection the latter frequency apparently relates to the C=O of the lactam group, if it is considered that a fairly constant range of $1670\text{--}1630\text{ cm}^{-1}$ has been established for N-disubstituted amides [7]. The same as the starting dipyrromethene (V), lactam (IX) exhibits in the region of the vibrations of the ring two bands of approximately equal intensity: at 1525 and at 1580 cm^{-1} . The fact that these bands, the same as in the case of (V), are approximately equal in intensity is understandable from the considerations discussed above for the case of compound (X), since in compounds (V) and (IX) both rings have the 2,4-type of substitution of the methyl groups, and the intensity of both bands of the stretching vibrations of the ring is multiplied by two.

As is true of most of the examined dipyrromethenes, existing in the methene form (V, VIII, XIV), compound (IX) fails to show absorption in the region of the C = C double bond ($1600-1680\text{ cm}^{-1}$). The fact that the bridging double bond does not show any substantial absorption can be explained by its central position and the complexity of

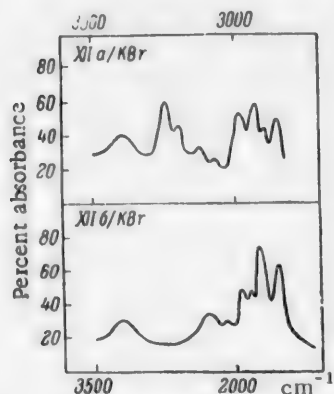


Fig. 3. Infrared absorption spectra. XIIa and XIIb) Molded into disks with KBr at 150 atm, in a vacuum of 0.1 mm.

the four substituents. On the other hand, all of the examined compounds, existing in the ethylene form (XIII, XI, X), exhibit substantial absorption in the 1600 cm^{-1} region, which relates to the ethylene bond in the side chain, present in the infrared spectrum because of the distinct asymmetry of the substitution in the present case, since the C = C becomes tri-substituted. Nevertheless, lactam (IX) should be assigned the ethylene form, for in the opposite case it would not exhibit the above mentioned clearly expressed absorption of the NH group. The presented considerations suggest that different conditions of symmetry exist in the molecule of compound (IX) than in the similar molecule of lactam (X), the spectrum of which shows a substantial intensity of the C = C band at 1620 cm^{-1} .

Compound (XII) is formed from compound (XI) when the cyclopentanone ring is closed by the Dieckmann procedure. Compound (XII) was isolated in two forms, differing in external appearance in that one form was orange and the other was yellow. The orange form (XIIa) exhibits in the NH region a quite intense band at 3240 cm^{-1} , whereas the yellow form (XIIb) fails to show noticeable absorption in this region, with the exception of a slight peak at 3100 cm^{-1} , the lower limit for the frequency of the NH group (see Fig. 3). It can be stated with a great deal of probability that a strong intramolecular bond is present in compound (XIIb). Since with its formation the possibilities of creating a similar bond for the other NH group, if it were present, are exhausted (a single carboxyl group was used up), while the spectrum fails to show the absorption of the free, or found in intermolecular association, NH group, then it becomes possible to make the second conclusion that (XIIb) exists in the methene form.

Both forms, (XIIa) and (XIIb), exhibit at 3400 cm^{-1} a broad band of medium intensity, the position and shape of which are not characteristic for the NH group in compounds in the solid state, where it usually absorbs in the limits $3300-3100\text{ cm}^{-1}$ [4]. It is most natural to relate this band to the absorption of the hydroxyl group, formed as the result of enolization of the keto group in the cyclopentanone ring; analogous absorption was manifested in the spectra of enolized β -diketones [8]. Enolization of compound (XII) is facilitated by the high activity of the hydrogen atoms located between the keto group and the carboxyl group. Judging by the similar intensity of the band at 3400 cm^{-1} , enolization takes place with equal ease for both (XIIa) and (XIIb); this suggests that (XIIa) also has the methene form, since in the opposite case of forming the ethylene form, the single free hydrogen atom, located between the keto and the carboxyl groups, would be consumed during rearrangement to form the second NH group, and enolization of the keto group would become impossible. The single assumption remains that two rotational isomers of compound (XII) exist, with a retention of the coplanarity of the system of conjugated rings. Both isomers will be characterized by a turning of one of the pyrrole rings by 180° .

The existence in the dipyrromethenes of stable space-rotational isomers is very important for the further synthesis of porphyrins.

An IKS-11 instrument was used to take the infrared spectra, operating with a NaCl prism in the $600-2000\text{ cm}^{-1}$ region, and using a LiF prism in the $2500-3500\text{ cm}^{-1}$ region.

SUMMARY

1. A study was made of the infrared spectra of a group of synthetically related dipyrromethenes with substituents in the meso-position.
2. It was established that these dipyrromethenes are inclined to show both intermolecular and intramolecular association.
3. It was found that a relationship exists between the intensity of the stretching vibrations of the ring and the position of the methyl substituents.
4. The existence of space-rotational isomers in the dipyrromethene series was shown.

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SYNTHETIC STUDIES IN THE VITAMIN B₆ GROUP

II. SYNTHESIS OF 2-METHYL-3-HYDROXY-4-AMINOMETHYL-5-HYDROXYMETHYLPYRIDINE

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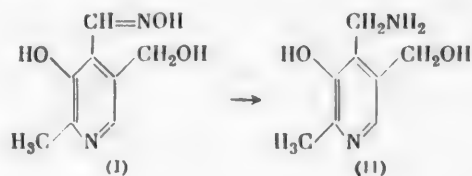
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Determination of the separate components of the vitamin B₆ group in natural sources [1, 2] revealed that the amount of pyridoxine reaches 20%, while the combined amount of pyridoxal and pyridoxamine reaches 80%. In view of this, the synthesis of pyridoxamine possesses definite interest.

However, the conversion of pyridoxine to pyridoxamine under laboratory conditions is accomplished with difficulty. Methods are known for obtaining pyridoxamine from pyridoxine diacetate [3] by treatment of the latter either with alcoholic ammonia solution at temperatures up to 110° or with liquid ammonia at 140°, in which connection the maximum yield does not exceed 7%. The reduction of 145 mg of pyridoxal oxime with hydrogen in the presence of platinum oxide and a pressure of 2 atm gave [3] only several milligrams of pyridoxamine. Karrer, Viscontini and Forster [4] reduced pyridoxal oxime in glacial acetic acid (50 fold amount) with hydrogen in the presence of 50% platinum oxide. The reduction took 5 hr, and the yield of pyridoxamine dihydrochloride was 87%. The reduction of pyridoxal oxime with zinc dust in glacial acetic acid [5] has the disadvantage that hydrogen sulfide has to be used to isolate the amine.

We developed a method for the reduction of pyridoxal oxime (I) to pyridoxamine (II) in dilute (1 : 25) hydrochloric acid, in the presence of 6% palladium chloride and 24% activated carbon. The reduction took 40-50 min. The yield of pyridoxamine dihydrochloride was 98.2%.



EXPERIMENTAL

2-Methyl-3-hydroxy-4-aminomethyl-5-hydroxymethylpyridine dihydrochloride (II, 2HCl). Into the hydrogenation apparatus were charged 0.24 g of activated carbon and 25 ml of distilled water, and then, after displacing the air by hydrogen, a solution of 0.06 g of palladium chloride in 2 ml of hydrochloric acid (d 1.18) was added in a stream of hydrogen. The reduction of the catalyst took 10-20 min, and here 35 ml of hydrogen was absorbed. Then 25 ml of ice-cold distilled water and 1 g of pyridoxal oxime (m.p. 215-215.5°) were added to the reduced catalyst. The reduction was continued for 45 min, and here 290 ml (calculated 261 ml) of hydrogen was absorbed. The catalyst was filtered, and the filtrate was evaporated in vacuo (10 mm). Yield 1.3 g (98.2%). M.p. 225-226° (from alcohol).

Found %: C 39.70; H 5.78; N 11.60; Cl 29.08. $C_8H_{12}O_2N_2 \cdot 2HCl$. Calculated %: C 39.81; H 5.84; N 11.62; Cl 29.41.

SUMMARY

A method was developed for the reduction of pyridoxal oxime with hydrogen at atmospheric pressure, in the presence of palladium catalyst, and using dilute hydrochloric acid as the solvent.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

LIPIDES

IX. SYNTHESIS OF SOME TRIGLYCERIDES OF SOYBEAN OIL

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Yu. B. Pyatnova, G. A. Serebrennikova,
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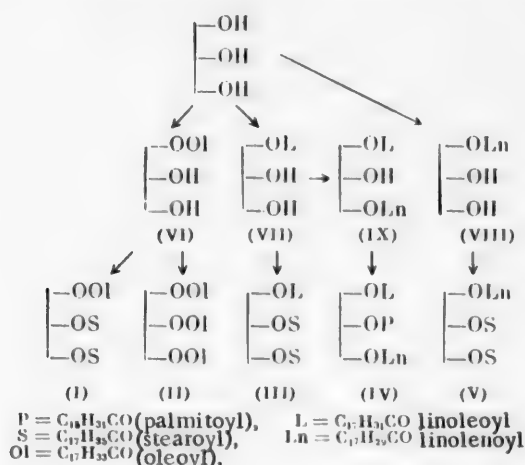
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The synthesis and principal physicochemical properties of α -oleoyl- β , α' -distearin (I), triolein (II), α -linoleoyl- β , α' -distearin (III), α -linoleoyl- β -palmitoyl- α' -linolenin (IV) and α -linolenoyl- β , α' -distearin (V), found in soybean and other plant oils, are described in the present paper. As in the previous communications [1-6], the triglycerides were obtained either by the direct esterification of the monoglycerides: α -monoolein (VI), α -monolinolein (VII) and α -monolinolenin (VIII) with stearoyl and oleoyl chlorides, in the case of compounds (I), (II), (III) and (V), or in two stages, for the triglyceride (IV), via α -monolinolein (VII) and α -linoleoyl- α' -linolenin (IX).



Paper chromatography and the infrared spectra were used to determine the purity of the triglycerides.

EXPERIMENTAL

α -Oleoyl- β , α' -distearin (I). A mixture of 35.8 g of α -monoolein (VI) and 25 ml of quinoline in 125 ml of chloroform was treated with 60.8 g of stearoyl chloride (b.p. 156-157°/0.5 mm, m.p. 22-23.5°). The reaction mass was heated under reflux in a nitrogen stream for 5 hr, after which it was cooled to 5-6°, treated with 250 ml of ether, and acidified with 50 ml of 10% sulfuric acid. The upper layer was separated, washed with saturated aqueous sodium bicarbonate solution, and dried over sodium sulfate. The solvent was vacuum-distilled (15 mm). The residue was washed with 80 ml of methyl alcohol at 40°, and then recrystallized twice from acetone (1 : 5) at -55 to -50°. Yield 26.3 g (28.3%).

After chromatographing through a column containing silica [7] (30 g of silica per gram of substance), m.p. 25-27°.

Found %: C 77.10; H 12.29. Iodine number 29.5. $C_{57}H_{108}O_6$. Calculated %: C 76.97; H 12.24. Iodine number 28.5.

Triolein (II). Using the method described for the synthesis of α -oleoyl- β , α' -distearin (I), from 40.4 g of α -monoolein (VI) and 30.5 g of quinoline in 200 ml of chloroform and 70.2 g of oleoyl chloride (b.p. 140-142°/0.5 mm), after two recrystallizations from acetone (1 : 5) at -30 to -28°, we obtained 50.5 g (51.0%) of triolein.

After chromatographing through a column containing silica:

M. p. 4-5°, d_4^{20} 0.9146, n_D^{20} 1.4676, MR_D 268.99. $C_{57}H_{104}O_6$ F₃. Calculated 268.63.

Found %: C 77.34; H 11.88. Iodine number 85.7. $C_{57}H_{104}O_6$. Calculated %: C 77.74; H 11.84. Iodine number 86.0.

α -Linoleoyl- β , α' -distearin (III). Using the same procedure as in the synthesis of (I), from 34.0 g of α -monoolein (VII) and 42.0 g of quinoline in 100 ml of chloroform and 95.0 g of stearoyl chloride, after removal of the impurities by washing 3 times with 50 ml portions of methyl alcohol at 40° and recrystallization from acetone (1 : 5) at -55 to -50°, we obtained 20.2 g (41.2%) of (III). M.p. 22-22.5°.

After chromatographing through a column filled with silica, m.p. 36-38°.

Found %: C 77.62; H 11.8. Iodine number 57.0. $C_{57}H_{106}O_6$. Calculated %: C 77.14; H 12.04. Iodine number 57.2.

α -Linoleoyl- β -palmitoyl- α' -linolenin (IV). The reaction of 18.6 g of α -linoleoyl- α' -linolenin (IX) with 9.5 g of palmitoyl chloride (b.p. 141-143°/0.4 mm) in 50 ml of chloroform, in the presence of 5.5 g of quinoline, gave, in the same manner as indicated for triglyceride (I), 18.6 g of technical product, which was recrystallized twice from acetone (1 : 5) at -60 to -55°, with prior separation of the fraction depositing at -12 to -10°. Yield 3.8 g (14.7%).

M. p. -(5-3)°, d_4^{20} 0.9479, n_D^{20} 1.4776, MR_D 251.6. $C_{55}H_{96}O_6$ F₅. Calculated 250.15.

Found %: C 77.69, 77.48; H 11.60, 11.26. Iodine number 151.6. $C_{55}H_{96}O_6$. Calculated %: C 77.39; H 11.34. Iodine number 148.7.

α -Linolenoyl- β , α' -distearin (V). From 6.1 g of α -monolinolenin (VIII) and 6.1 g of quinoline in 20 ml of chloroform and 10.6 g of stearoyl chloride, after washing with 85 ml of methyl alcohol at 40° and recrystallization from acetone (1 : 5) at -25 to -20°, we obtained 3.9 g (25.4%) of (V). M.p. 24.3-24.5°.

After chromatographing through a column filled with silica, m.p. 31-31.5°.

Found %: C 77.66; H 11.60. Iodine number 86.6. $C_{57}H_{104}O_6$. Calculated %: C 77.32; H 11.84. Iodine number 86.0.

SUMMARY

The synthesis of α -oleoyl- β , α' -distearin, triolein, α -linoleoyl- β , α' -distearin, α -linoleoyl- β -palmitoyl- α' -linolenin and α -linolenoyl- β , α' -distearin was accomplished.

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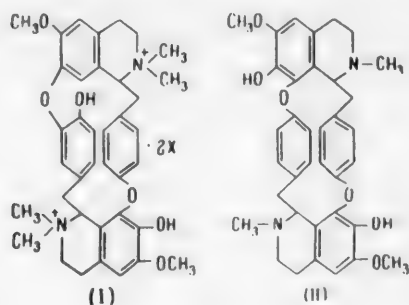
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THE ULTRAVIOLET SPECTRA AND STRUCTURE OF DIPHENYL ETHERS

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In previous papers we described the synthesis of a series of substituted diphenyl ethers, which could be regarded as being structural elements of the curare alkaloids—tubocurarine (I), isochondrodendrine (II), and others.



A study of the spectra of these compounds and their dependence on the character and position of the substituents possesses definite interest. Studies of this type have been made only with the simpler diphenyl ethers [1-5]. Our studies with the substituted diphenyl ethers [6-9] disclosed the peculiarities of their structure as a function of the substituents (see table).

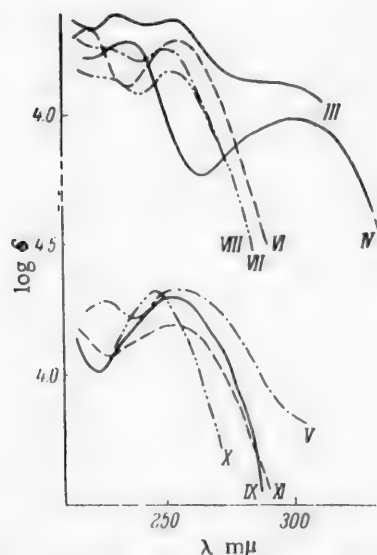
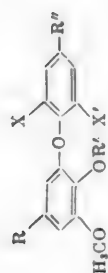


Fig. 1. Ultraviolet absorption spectra of compounds (III)-(XI). The numbers of the curves correspond to the numbers of the compounds in the text and in the table.

Thus, for example, the ultraviolet spectrum of 2-hydroxy-3-methoxy-5-formyl-4'-carboxydiphenyl ether (III) shows a broad absorption region with three maxima: at 237, 254 and 290 $m\mu$. The middle maximum, corresponding to the absorption in 4-phenoxybenzoic acid [3], can be explained by the quinoid structure of the lower ring, caused by the carboxyl group found in the 4'-position and the unshared electron pair of the ether oxygen atom. Because of this, the bonds ($C-O-C_1$) of the oxygen stretching angle should be found in the plane of the conjugated ring. A similar phenomenon was observed for the 4-nitrophenyl ethers [10, 11], in which connection the molecule can be drawn out of the coplanar state by introducing two large substituents in the ortho-position to the ether linkage. The absence of such conjugation in the homologous acid (IV) is naturally accompanied by the disappearance of the middle maximum on the absorption curve of the latter compound.

The maximum at 290 $m\mu$ testifies to the quinoid structure of the vanillyl ring in diphenyl ether (III), confirmed by the fact that this maximum vanishes when its phenolic hydroxyl is methylated or acetylated to compounds (V) and (VI). With a simultaneous acetylation of the aldehyde group in compounds (VII) and (VIII),



Diphenyl ether	Fig. no.	R	R'	R''	X	X'	1		2		3		Method of preparation	Literature reference
							λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$		
III	1	CHO	H	COOH	H	H	237	4.325	254	4.325	290	4.129	Obtained from compound (VII) by the Arndt-Eistert procedure. M.p. 50-60°	[8] [7]
IV	1	CHO	H	CH ₂ COOH	H	H	235	4.297	—	—	295	3.985		
V	1	CHO	CH ₃	COOCH ₃	H	H	225	4.284	255	4.330	—	—	Obtained from the methyl ester of (XIII) by removal of the nitro group. M.p. 142-143°	[8] [7]
VI	1	CHO	COCH ₃	COOCH ₃	H	H	225	4.267	255	4.298	—	—		
VII	1	CH(OCOCH ₃) ₂	COCH ₃	COOH	H	H	—	—	250	4.265	—	—	Obtained by the acetylation of compound (III) in conventional manner. M.p. 196-198°	[7] [6] [8]
VIII	1	CH(OCOCH ₃) ₂	COCH ₃	COOCH ₃	H	H	—	—	253	4.164	—	—	Obtained in a similar manner from compound (VI). M.p. 119-121°	
IX	1	CH ₃	CH ₃	COOCH ₃	H	H	—	—	252	4.296	—	—	Obtained from compound (VII) by the Arndt-Eistert procedure. M.p. 50-60°	[7] [6] [8]
X	1	CH ₂ OH	CH ₃	COOCH ₃	H	H	—	—	245	4.324	—	—		
XI	1	CH ₂ CH ₂ NH ₂	H	COOC ₂ H ₅	H	H	—	—	252	4.194	—	—	Obtained from compound (VI). M.p. 119-121°	[7] [6] [8]
XIII	2	CH(OCOCH ₃) ₂	COCH ₃	COOH	NO ₂	H	225	4.346	—	—	305	3.362		

Diphenyl ether	Fig. no.	R	R'	R''	X	X'	1		2		3		Method of preparation	Literature reference
							λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$		
XIV	2	COOCH ₃	CH ₃	COOCH ₃	NO ₂	H	225	4.194	253	4.184	295	3.739	Obtained from the methyl esters of 2,3-dimethoxy-4-bromobenzoic acid in pyridine. Yield 31.7%. M.p. 131-133° (from alcohol).	[9]
XV	2	COOCH ₃	CH ₃	CH(OCOCH ₃) ₂	NO ₂	H	225	4.435	250	4.082	295	3.672	Obtained by the acetylation of 2,3-dimethoxy-2'-nitro-4'-formyl-5-carbomethoxydiphenyl ether. M.p. 70-72°.	[9]
XVI	2	CHO	H	CH ₂ COOH	NO ₂	NO ₂	225	4.716	—	—	295	4.374		[9]
XVII	2	CHO	H	CH ₂ COOCH ₃	NO ₂	NO ₂	225	4.523	—	—	295	4.187		[9]
XVIII	2	CH(OCOCH ₃) ₂	COCH ₃	CH ₂ COOCH ₃	NH ₂	NO ₂	225	4.524	—	—	280	3.623		[9]
XIX	2	CH(OCOCH ₃) ₂	COCH ₃	CH ₂ COOCH ₃	NHCOCH ₃	NHCOCH ₃	225	4.576	—	—	280	3.580		[9]
XX	2	CH(OCOCH ₃) ₂	COCH ₃	CH ₂ COOH	NO ₂	NO ₂	225	4.585	—	—	300	3.787		[9]
XXI	3	CH(OCOCH ₃) ₂	COCH ₃	CH ₂ COOCH ₃	I	NHCOCH ₃	226	4.490	—	—	—	—		[9]
XXII	3	CHO	H	CH ₂ COOH	I	NHCOCH ₃	225	4.385	—	—	300	4.086		[9]
XXIII	3	CHO	H	CH ₂ COOCH ₃	I	NHCOCH ₃	225	4.594	—	—	300	4.098		[9]
XXIV	3	CH=CHNO ₂	H	COOH	H	H	—	—	252	4.317	367	4.206		[8]

and also when the latter is replaced by the methyl, hydroxymethyl or aminoethyl group in compounds (IX)-(XI), together with a disappearance of the third maximum, the first maximum shifts toward the short-wave region. Ap-

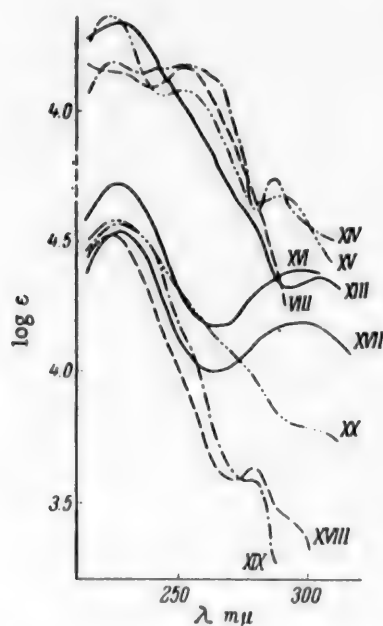


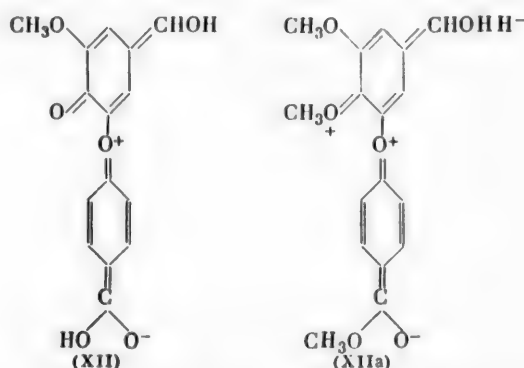
Fig. 2. Ultraviolet spectra of compounds (XIII)-(XX). The curve of compound (VIII) is shown for comparison.

parently, this is also associated with a disturbance of the coplanar quinoid structure of the upper ring.

As a result, the spectra of compounds (III) and (V) can be explained by the existence of two not connected conjugated systems in the molecule, as can be seen in the structures (XII) and (XIIa).

The absence of a single conjugated system in the indicated compounds is in agreement with the fact that aromatic rings are located in perpendicular planes [12].

The presence of one nitro group in the ortho-position to the ether linkage is apparently without steric effect on the coplanarity of the molecule. However, there is noticeable interaction of the nitro group with the ether oxygen, leading to the appearance of a slight maximum in the 290-305 mμ region, for example, in compounds (XIII)-(XV).



Inflections in the 250 mμ region are observed in the spectra of compounds (XVII)-(XXIII), explained by alterations of the conjugations in the rings due to the formation of intramolecular hydrogen bonds, causing a change in the angle between the planes of the rings.

Lengthening the chain of conjugation in the upper ring causes the third maximum to shift toward longer wavelengths, not changing the conjugation of the lower ring. Thus, for example, 2-hydroxy-3-methoxy-5-(β-nitrovinyl)-

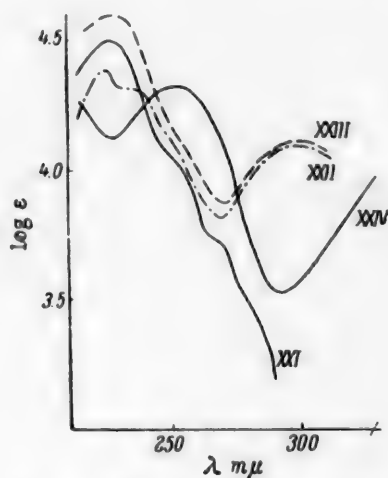


Fig. 3. Ultraviolet spectra of compounds (XXI)-(XXIV).

4'-carboxydiphenyl ether (XXIV) exhibits maxima at 252 and 367 m μ , characteristic for compound (III) and ω -nitrostyrenes.

All of the spectra of the diphenyl ethers were taken with an SF-4 spectrophotometer, in 96% alcohol solution, at a concentration ranging from $0.8 \cdot 10^{-4}$ to $1.5 \cdot 10^{-4}$ M.

SUMMARY

1. A study was made of the relationship existing between the absorption spectra of a number of diphenyl ether derivatives, functioning as intermediates in the synthesis of curare alkaloids, and their structure.
2. It was shown that diphenyl ethers, containing a carboxyl group in the 4'-position, and also having the vanillyl radical, possess a quinoid structure.
3. Both rings behave independently of each other, which serves as evidence that the rings are in perpendicular planes.

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CONCERNING COLOR IN THE SERIES OF 2-CHROMONE-CARBOXYLIC ACID DERIVATIVES

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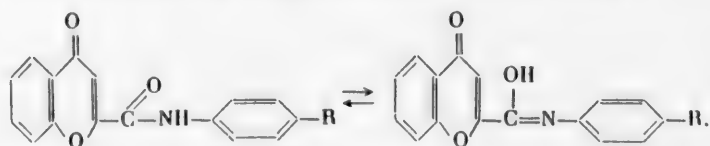
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In a previous paper [1] we discussed the influence of various substituents in the aryl radical of the arylides of 2-chromonecarboxylic acid on the long-wave limit of absorption. A comparison of the absorption spectra of the N-methyl-p-hydroxyanilide ("fixed" form, not capable of enolization) and p-hydroxyanilide of 2-chromonecarboxylic acid disclosed a substantial reduction in the absorption of the first compound, especially in the long-wave region. This led to the thought that the reason for the appearance of color in the anilides of 2-chromonecarboxylic acid is the formation of a system of conjugated bonds via the isomerization of the CONH group:



However, an examination of the literature data placed in doubt the theory that enolization of the CONH bridge is exclusively responsible for the formation of deeply colored compounds. Actually, a deep color may be observed not only in the case of interaction of the electron-donor (AK) and electron-acceptor (KB) portions of the molecule via the completely conjugated system of double bonds (Q), but also when the grouping Q-AK-Q-KB breaks the chain of conjugation [2-8] ($Q = \text{CH}_2$, $(\text{CH}_2)_n\text{NH}$, $\text{C}(\text{C}_6\text{H}_5)_2$, $\text{CH}_2\text{CH}_2\text{COO}$, etc.).* The indicated authors associate the main reason for color with the presence of a direct intermolecular reaction (complex-formation), which is dependent on the degree of electrophilicity and electronegativity of the systems A and B. At the same time, with the CONH bridge present, the possibility of a conjugated system of bonds arising as the result of isomerization of the given grouping is not excluded. For example, this was observed for the substituted (OCH_3 , OH, and $\text{N}(\text{CH}_3)_2$) anilides of the mono- and dinitrobenzoic acids [10]. Here a correlation was usually observed between the state of the color in the solid and in solution [11, 13]. In the case of the indicated compounds, going from the mononitro to the dinitro derivatives is accompanied, as a rule, by a deepening of the color. In solution, for example, the band for the absorption of the p-dimethylaminoanilide of p-nitrobenzoic acid in the long-wave region is found at $380 \text{ m}\mu$ [12], while the corresponding anilide of 2,4-dinitrobenzoic acid exhibits a band at $400 \text{ m}\mu$ [13].

The additional introduction into the bridge of from one to three methylene units (anilides of phenylacetic, dihydrocinnamic and phenylbutyric acids) causes a heightening of the color for the corresponding compounds in the crystalline state [14, 15], while in solution [12] the indicated factor facilitates a vanishing of the color at dilutions of the order of $1 \cdot 10^{-3} - 1 \cdot 10^{-4} \text{ M}$.

The question of color in compounds of type AK-Q-KB, where the chromonoyl radical is present as the electrophilic system (KB), is not discussed in the literature.

We synthesized some N-substituted amides of 2-chromonecarboxylic acid where isomerization of the amido grouping could not lead to conjugation between the substituted phenyl radical and the chromone system (Ia-c, table).

* In its influence on color the CONH group occupies an intermediate position between the $-\text{CH}=\text{CH}-$ and $-\text{CH}_2\text{CH}_2-$ groups [9].

<table><tr><th>compound</th></tr><tr><td>Ia</td></tr><tr><td>Ib</td></tr><tr><td>Ic</td></tr></table>	compound	Ia	Ib	Ic	<table><tr><th>R</th></tr><tr><td>H</td></tr><tr><td>OCH₃</td></tr><tr><td>N(CH₃)₂</td></tr></table>	R	H	OCH ₃	N(CH ₃) ₂	<table><tr><th>color</th></tr><tr><td>Colorless</td></tr><tr><td>Nearly colorless</td></tr><tr><td>Bright lemon-yellow</td></tr></table>	color	Colorless	Nearly colorless	Bright lemon-yellow
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compound														
IIIa														
IIIb														
IIIc														
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N(C ₂ H ₅) ₂														
color														
Colorless														
Bright yellow														
Red														

Separating the NH group from the double bonds of the phenyl moiety by two methylene units causes a substantial heightening of the color for compounds (Ia-c) when compared with compounds (IIa-c), described previously [1]. Nevertheless, a bright lemon-yellow color is observed for (Ic). The absorption spectra (Fig. 1) also testify to the deep changes that took place in the solutions of compounds (Ia-c) when compared with compounds (IIIa-c), especially in the visible region. The color of the solutions of the (III) compounds (see [1]), deepening with increase in the electronegativity of the R substituent, is, in general, absent in the case of compounds of type (I). Compounds (Ia, b) each exhibit two maxima in the ultraviolet region of the spectrum – a short-wave maximum at 236 and 237 mμ (log ε 4.28 and 4.42, respectively), and a long-wave maximum at 304-306 mμ (log ε 3.81 and 3.89, respectively). In this region the spectrum of compound (Ic) (the same as the spectrum of compound IIIc) exhibits three absorption bands, two of which (at 236 mμ, log ε 4.43, and 304 mμ, log ε 3.99), as had been proposed by us earlier [1], are associated with the presence of the chromone system. The third maximum is located at 255 mμ. Its intensity (log ε 4.44) is the greatest and substantially exceeds the intensity of the band for (IIIc) in the same region (λ 261 mμ, log ε 4.28 [1]).



Fig. 1. Ultraviolet absorption spectra of amides of 2-chromonecarboxylic acid. 1) N-Phenylethylamide (Ia); 2) N-(p-methoxyphenylethyl)amide (Ib); 3) N-(p-dimethylaminophenylethyl)amide (Ic).

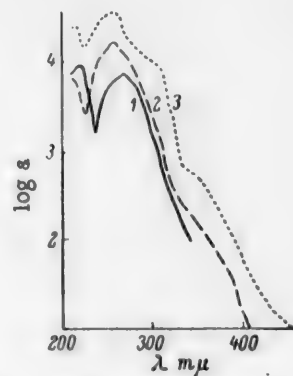


Fig. 2. Ultraviolet absorption spectra of amides of p-nitrobenzoic acid. 1) N-Phenylethylamide (IIa); 2) N-(p-methoxyphenylethyl)amide (IIb); 3) N-(p-dimethylaminophenylethyl)amide (IIc).

In order to compare the chromonoyl and p-nitrobenzoyl derivatives, containing the CONHCH₂CH₂ bridge, in their ability to give colored compounds, we synthesized compounds (IIa-c) (table), where the sequence of the groupings CONH and CH₂CH₂ was the same as in the case of (Ia-c).

We found that the color of compounds (IIa-c) was comparable with that of the corresponding dihydrocinnamic acid derivatives, having the indicated groups arranged in the reverse order [12, 14, 15]. Consequently, the order in which the amido group and the methylene units are arranged in the p-nitrobenzoyl derivatives is probably without important effect on the depth of color.

In the visible region, compounds (IIa-c) in solution (Fig. 2) behave like compounds (Ia-c). This indicates that the colored complexes are destroyed under the influence of the solvent. The presence of "tails" in the spectra (especially for compounds IIa-c, where $\log \epsilon$ is 1.8 at λ 400 m μ) is possibly due to residual complex-formation.

As a result, from a comparison of the literature data with our results it can be concluded that when going from compounds with a CONH bridge to compounds with a CONHCH₂CH₂ bridge the chromonoyl and p-nitrobenzoyl radicals, in general, behave in the same manner as regards the effect on color (a heightening of the color in the solid state, and a disappearance of the color in solutions). Nevertheless, mention should be made of the somewhat smaller capacity shown by the chromonoyl moiety, when compared with the p-nitrobenzoyl radical, to produce color in the series of separated systems (see table, compounds Ia-c and IIa-c). In contrast to this, in compounds containing the CONH bridge, the influence of the chromonoyl moiety on the deepening of the color of the compounds in solution apparently exceeds the influence of the p-nitrobenzoyl radical and approaches that of the 2,4-dinitrobenzoyl radical in this respect.

EXPERIMENTAL*

An SF-4 quartz spectrophotometer was used to measure the absorption spectra. Rectified alcohol, previously distilled through a fractionating column, was used as the solvent. The concentration of the solutions ranged from $1 \cdot 10^{-3}$ to $0.2 \cdot 10^{-4}$ M.

N-Phenylethylamide of 2-chromonecarboxylic acid (Ia). The compound was obtained in 78% yield from 2-chromonecarbonyl chloride and phenylethylamine, by the method described for the p-toluidide [16]. M.p. 173-174° (from alcohol).

Found %: C 74.16, 74.15; H 5.10, 5.03; N 4.73, 4.89. C₁₈H₁₅O₃N. Calculated %: C 73.67; H 5.15; N 4.79.

N-(p-Methoxyphenylethyl)amide of 2-chromonecarboxylic acid (Ib). p-Methoxy- ω -nitrostyrene, m.p. 85-87°, obtained by the condensation of p-methoxybenzaldehyde with nitromethane [17], was reduced with aluminum lithium hydride to p-methoxyphenylethylamine, by the method described for the m-isomer [18]. Yield 50%. B.p. 113-115° (6-7 mm). Literature data [19]: b.p. 136-138° (18 mm).

The amide (Ib) was synthesized in the same manner as the preceding; yield 74%, m.p. 206-206.5° (from alcohol).

Found %: C 70.61, 70.47; H 5.31, 5.24; N 4.41, 4.26. C₁₉H₁₇O₄N. Calculated %: C 70.56; H 5.29; N 4.32.

N-(p-Dimethylaminophenylethyl)amide of 2-chromonecarboxylic acid (Ic). p-Dimethylamino- ω -nitrostyrene, m.p. 182-183° [17], was reduced with aluminum lithium hydride [20] to p-dimethylphenylethylamine, b.p. 98-100° (1 mm). From the literature [20]: b.p. 116-117° (2-3 mm).

The amide (Ic) was obtained in the same manner as before (the reaction product was not washed with hydrochloric acid), yield 80%, m.p. 189-190.5° (from alcohol).

Found %: C 71.25, 71.16; H 5.92, 5.89. C₂₀H₂₀O₃N₂. Calculated %: C 71.37; H 5.99.

N-(Phenylethyl)amide of p-nitrobenzoic acid (IIa). Obtained from p-nitrobenzoyl chloride and phenylethylamine, in the same manner as compound (Ia); yield 60%, m.p. 144-145°. From the literature [21]: m.p. 147°.

N-(p-Methoxyphenylethyl)amide of p-nitrobenzoic acid (IIb). Synthesized in the same manner as described above; yield 89%, m.p. 147-147.5° (from alcohol). From the literature [21]: m.p. 145°.

N-(p-Dimethylaminophenylethyl)amide of p-nitrobenzoic acid (IIc). Obtained in the same manner as amide (Ic); yield 94%, m.p. 218-219° (from butanol).

Found %: C 65.33, 65.37; H 6.18, 6.26; N 13.37, 13.33. C₁₇H₁₉O₃N₃. Calculated %: C 65.11; H 6.10; N 13.47.

SUMMARY

1. To study the color in the series of the amides of 2-chromonecarboxylic acid we synthesized the N-phenylethylamide, N-(p-methoxyphenylethyl)amide and N-(p-dimethylaminophenylethyl)amide of 2-chromonecarboxylic acid. For comparison purposes, we also synthesized the corresponding anilides of p-nitrobenzoic acid.

2. It was established that color can appear in amides of 2-chromonecarboxylic acid containing separated electrophilic and electron-donor systems (CONHCH₂CH₂ bridge). This indicates that enolization of the amido group in the anilides of 2-chromonecarboxylic acid (CONH bridge) is not a necessary condition for the creation of color.

* With the assistance of N. D. Solokhina.

3. It was observed that an analogy exists in the behavior of the chromonoyl and p-nitrobenzoyl radicals as regards the influence on the color when going from compounds with a CONH bridge to compounds with a CONHCH₂CH₂ bridge.

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SULFO ESTERS OF STEROLS AND THEIR TRANSFORMATIONS

A. M. Khaletskii and M. V. Vasil'eva

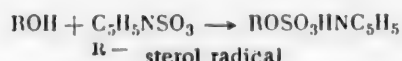
Leningrad Institute of Pharmaceutical Chemistry

Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

pp. 2996-3000, September, 1961

Original article submitted September 15, 1960

The acid sulfoesters of cholesterol and its analogs may be obtained by reacting pyridinesulfotrioxide with sterols [1].

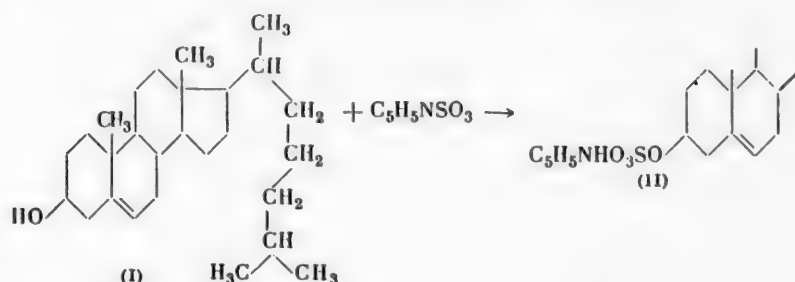


The reaction goes quite smoothly and with good yields in anhydrous organic solvents at 30-60° [2]. Later the sulfoesters of cholesterol were obtained in chloroform medium at room temperature [3]. Small amounts of cholesterol were isolated from biological material by reacting chlorosulfonic acid with cholesterol in carbon tetrachloride medium in the presence of pyridine [4].

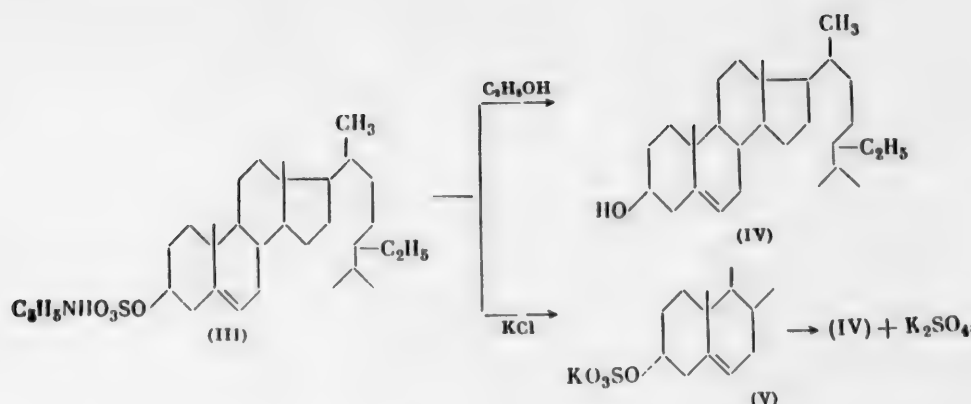
Attention to the sulfo esters has been attracted by the interesting properties of these compounds; thus, when halides and other salts are reacted with cholesterol pyridine sulfates the pyridine radical is easily replaced by the metal with the formation of the potassium, sodium and other salts of the sulfoesters of cholesterol. The ester linkage in steryl sulfates is quite stable in both acid and alkaline media at room temperature and is destroyed only when heated with acids [5]. As a result, the pyridine radical may serve as a reliable protective agent for the hydroxyl group in oxidation reactions. The reaction of diazomethane with pyridinium cholesteryl sulfate gave methyl cholesteryl sulfate [6].

Although the method for the preparation of steryl sulfates is not complicated, still it requires large amounts of absolutely anhydrous solvents. For this reason the method developed by us for the preparation of steryl sulfates by the fusion of the sterol with pyridinesulfotrioxide at 140-150° possesses interest; however, with our method it is impossible to obtain the dibromo derivatives of the steryl sulfates in view of the great sensitivity of the dibromides to heat.

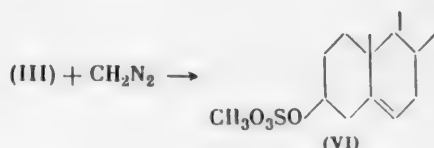
Of the sterols of animal origin this method was checked on cholesterol (I), which when fused with pyridine - sulfotrioxide at 150° was converted in good yield to pyridinium cholesteryl sulfate (II).



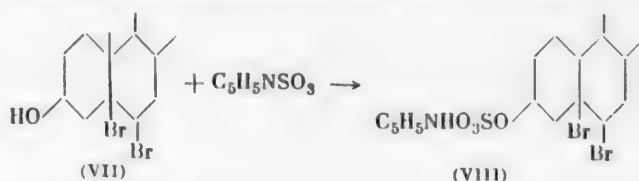
Of the sterols of plant origin we obtained pyridinium β-sitosteryl sulfate by heating β-sitosterol, isolated from the waste of cellulose production [7], with pyridinesulfotrioxide at 140°. Pyridinium β-sitosteryl sulfate (III) is a white crystalline powder, giving a positive Liebermann-Burchard reaction and a negative test with digitonin. When boiled with alcohol, sulfate (III) is cleaved with the formation of β-sitosterol (IV), but when it was treated with aqueous potassium chloride solution the potassium salt (V) was isolated, which when heated in refluxing dioxane is cleaved to β-sitosterol and potassium sulfate.



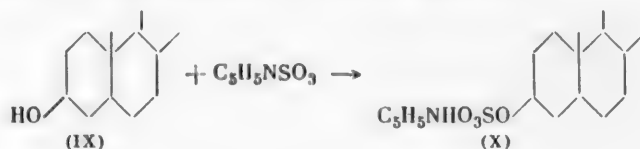
The methyl ester of β -sitosteryl sulfate (VI) was isolated when pyridinium β -sitosteryl sulfate was reacted with diazomethane.



The reaction of 5,6-dibromositosterol (VII) with pyridinesulfotrioxide at 30-35° in absolutely anhydrous solvents gave the dibromo derivative (VIII), which, in contrast to 5,6-dibromo- β -sitosterol, is quite stable and can be kept in a vacuum-desiccator for a long time without noticeable decomposition.



The fusion of dihydro- β -sitosterol with pyridinesulfotrioxide gave pyridinium dihydro- β -sitosteryl sulfate (X), which in its properties proved to be close to pyridine β -sitosteryl sulfate.



EXPERIMENTAL

Pyridinium cholesteryl sulfate (II). A mixture of 2 g of cholesterol and 2 g of pyridinesulfotrioxide was heated in an oil bath at 135° for 5-7 min and then for another 3-5 min at 150°. The yellow friable mass was cooled to 30° and then treated with 35 ml of chloroform, in which connection the pyridinium cholesteryl sulfate went into solution, while the excess pyridinesulfotrioxide separated as a white crystalline powder, and after keeping at 0° for 30 min, was filtered. The addition of 80 ml of petroleum ether (b.p. 60-80°) to the filtrate gave a white deposit, which after cooling for 1-2 hr was filtered; we obtained 2.1 g (80%) of substance with m.p. 175-177°. After recrystallization from a mixture of chloroform and petroleum ether, m.p. 178° (with decompn.); the compound crystallizes with 1 mole of chloroform, which is cleaved when the compound is kept in a vacuum-desiccator for 6-7 days.

Found %: S 5.00, 4.75. Equiv. 660. $\text{C}_{32}\text{H}_{51}\text{O}_4\text{NS} \cdot \text{CHCl}_3$. Calculated %: S 4.81. Equiv. 665.

Pyridinium β -sitosteryl sulfate (III). A mixture of 2 g of β -sitosterol and 2 g of pyridinesulfotrioxide was fused at 140°; we obtained 2 g (70%) of a white crystalline powder, m.p. 178-180° (with decompn.). After reprecipitation from a mixture of chloroform and petroleum ether (1 : 1) and storage in a vacuum-desiccator for 5-7 days, m.p. 184-185° (with decompn.).

Found %: S 5.51, 5.42. Equiv. 570. $C_{34}H_{55}O_4NS$. Calculated %: S 5.58. Equiv. 574.

The compound is readily soluble in chloroform, ethyl and methyl alcohols, and pyridine, less readily soluble in benzene and toluene, and insoluble in petroleum ether. It gives a gelatinous solution in hot water. It gives a positive Liebermann-Burchard reaction and a negative test with digitonin.

Cleavage of pyridinium β -sitosteryl sulfate. A mixture of 1 g of the sulfate (III) and 50 ml of 96% alcohol was heated under reflux for 3 hr, after which the solution was cooled, diluted with 50 ml of water, and the obtained precipitate was filtered; we obtained 0.52 g (71%) of substance. After recrystallization from alcohol, m.p. 138-139°. The compound gives a positive Liebermann-Burchard reaction, a positive test with digitonin, and a negative test for nitrogen and sulfur. The mixed melting point with authentic β -sitosterol was not depressed.

Potassium salt of pyridinium β -sitosteryl sulfate (V). A mixture of 1 g of sulfate (III) and 20 ml of water was treated with 20 ml of 10% potassium chloride solution; the obtained white flocculent precipitate was filtered and then washed with water, alcohol, chloroform, and ether; we obtained 0.7 g (73%) of a white crystalline powder. After recrystallization from 70% methyl alcohol, m.p. 216° (with decompn.); the compound is insoluble in chloroform and ether, and is soluble in alcohols. It crystallizes with 1 mole of water.

Found %: K 6.96, 7.06. $C_{29}H_{48}O_4SK \cdot H_2O$. Calculated %: K 7.10.

Cleavage of potassium salt of β -sitosteryl sulfate. A mixture of 0.5 g of the salt (V) and 50 ml of dioxane was heated under reflux for 10-15 min, after which the solution was diluted with 100 ml of water and the obtained precipitate was filtered; we obtained 0.35 g (95%) of the compound. After two recrystallizations from alcohol, m.p. 137-138°. The compound gives a positive Liebermann-Burchard reaction and a positive test with digitonin.

The mixed melting point with authentic β -sitosterol was not depressed.

Methyl ester of β -sitosteryl sulfate (VI). An ether solution (75 ml) of diazomethane, obtained from 3.5 g of nitrosomethylurea [8] was added with stirring to 5 g of sulfate (III) in 400 ml of chloroform. The reaction product was washed first with 400 ml of 0.01 N hydrochloric acid solution, then with the same amount of 0.01 N sodium bicarbonate, and finally with water. The ether-chloroform layer was separated from the aqueous layer, dried over fused sodium sulfate, and the solvent was vacuum-distilled. The dry residue was dissolved in 30 ml of ether, the insoluble portion was filtered, and the ether filtrate was evaporated; we obtained 2 g (52%) of substance with m.p. 105-106° (with decompn.). The compound is readily soluble in organic solvents and is insoluble in water. The compound contains sulfur, gives a positive Liebermann-Burchard reaction, and a negative test with digitonin.

Found %: S 6.37, 5.88. $C_{30}H_{52}O_4S$. Calculated %: S 6.28.

Pyridinium 5,6-dibromo- β -sitosteryl sulfate (VIII). Into a flask, fitted with a reflux condenser, protected from atmospheric moisture, and a stirrer were charged 50 ml of dry benzene and 4 g of 5,6-dibromo- β -sitosterol, obtained by the bromination of β -sitosterol with tetrabromopyridine in chloroform solution [9]. Then 5 ml of acetic anhydride, 5 ml of dry pyridine and 4 g of pyridinesulfotrioxide were added to the reaction mixture. The mixture was heated in a water bath for 30 min at 30-32°, cooled to 15°, and stirred with 200 ml of petroleum ether (b.p. 60-80°). After keeping in the refrigerator at 0° for 1 hr the precipitate was filtered and washed twice with a mixture of benzene and petroleum ether (1 : 5). To remove the pyridinesulfotrioxide, the precipitate was dissolved in 25 ml of chloroform and again placed in the refrigerator for 30 min at 0°. After filtering the deposited pyridinesulfotrioxide, the chloroform filtrate was treated with 100 ml of petroleum ether (b.p. 60-80°) and the newly obtained white precipitate was filtered after keeping for 2 hr at 0°. After drying in a vacuum-desiccator, we obtained 3.26 g (64%) of substance with m.p. 134-135° (with decompn.).

Found %: S 4.12, 4.26. $C_{34}H_{53}O_4NSBr_2$. Calculated %: S 4.37.

The compound is a white crystalline powder, readily soluble in chloroform, and more difficultly soluble in benzene and toluene; it dissolves in hot water with the formation of a gelatinous solution. A yellowing of the compound is observed when stored for several weeks.

Pyridinium dihydro- β -sitosteryl sulfate (X). A mixture of 0.65 g of dihydro- β -sitosterol, isolated from 20 g of β -sitosterol by treating the latter with a mixture of acetic anhydride and concentrated sulfuric acid in chloroform [9], and 0.65 g of pyridinesulfotrioxide was fused at 140° for 3-5 min. The reaction product was dissolved in 15 ml of chloroform and the excess pyridinesulfotrioxide was removed by filtration. After washing with 50 ml of petroleum ether, the precipitate was filtered and dried in a vacuum-desiccator; we obtained 0.6 g (72%) of (X) as a white crystalline powder. After two reprecipitations from a mixture of chloroform and petroleum ether (1 : 1), followed by long standing in a vacuum-desiccator, the substance gave a negative test for halogen and melted at 188-190° (with decomposition.).

Found %: S 5.38, 5.42. Equiv. 560. $C_{34}H_{57}O_4NS$. Calculated %: S 5.56. Equiv. 576.

The compound is soluble in chloroform and ethyl and methyl alcohols, less readily soluble in benzene and toluene, and insoluble in petroleum ether.

SUMMARY

1. Using cholesterol and β -sitosterol as examples, it was shown that it is possible to synthesize the 3-sulfo esters by fusing the sterols with pyridinesulfotrioxide at 140-150°.

2. A study was made of the properties of pyridinium β -sitosteryl sulfate and its derivatives.

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INVESTIGATIONS ON THE CHEMISTRY OF 2,1,3- THIA- AND SELENADIAZOLE

XII. SYNTHESIS AND STUDY OF PYRIMIDO-2,1,3-SELENADIAZOLE DERIVATIVES

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pp. 3000-3003, September, 1961

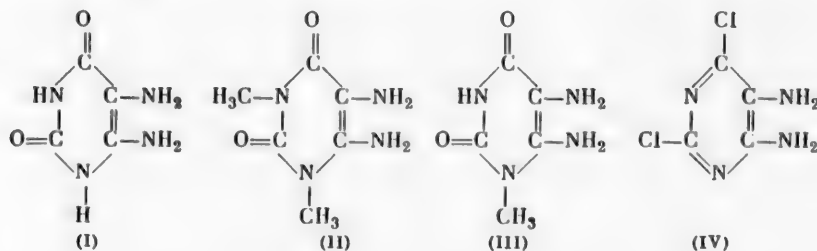
Original article submitted September 15, 1960

In a previous paper [1] we presented some data relating to the synthesis and study of pyrimido-2,1,3-thiadiazole derivatives; the latter, as was revealed by biological testing [2], exert a certain activity in inhibiting the growth of Ehrlich tumors in mice. Consequently, it seemed of interest to study the biological activity of the pyrimido-2,1,3-selenadiazole derivatives, since some recently published data [3, 4] clearly show that organoselenium compounds play an important role in the metabolic activity of the organism. The high toxicity displayed by organoselenium compounds, as a result of which they have failed to find use in medicine [5], is not a serious argument against seeking for new drugs in this series of compounds; as is known, some organophosphorus compounds, showing a higher toxicity toward warm-blooded animals, have proved to be extremely effective [6].

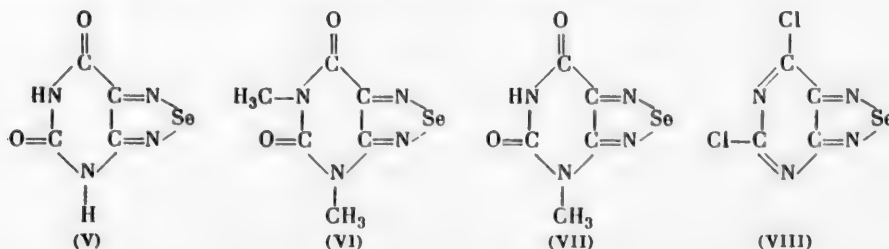
In a number of respects the 2,1,3-selenadiazole derivatives are quite different from the corresponding thio analogs, although in its electronegativity selenium lies close to sulfur (the electronegativity of sulfur is 2.5, and that of selenium is 2.4 ev [7]). In view of this, a comparison of the reactivity of 2,1,3-selena- and thiadiazole derivatives is fully in order.

In this paper we describe the data obtained in studying the reaction of some 4,5-diaminopyrimidines with selenium dioxide and the chemical properties of the obtained pyrimido-2,1,3-selenadiazole derivatives.

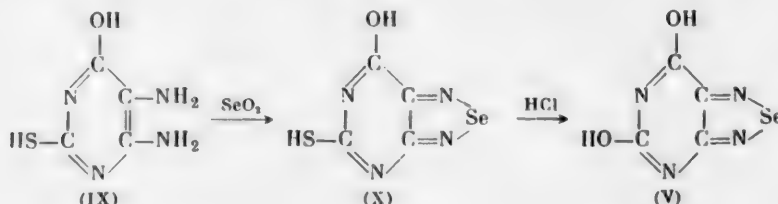
When the reaction is run with o-diamines (I-IV) [8]:



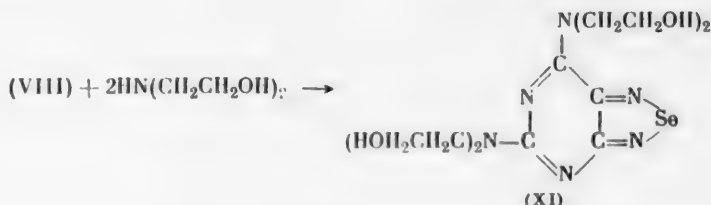
The process goes in the same manner as with aromatic o-diamines; diamines (I-IV) react with selenium dioxide to give the corresponding 2,1,3-selenadiazole derivatives (V-VIII) in good yield.



2-Mercapto-6-hydroxy-4,5-diaminopyrimidine (IX) also enters into the given reaction to yield, as might be expected, 4-hydroxy-6-mercaptopyrimido-2,1,3-selenadiazole (X), but the latter cannot be purified by the usual procedures. Recrystallization of the technical product from hydrochloric acid apparently results in hydrolysis, leading to the formation of 4,6-dihydroxypyrimido-2,1,3-selenadiazole (V); a similar conversion of the mercapto or alkyl-mercapto group when treated with acids is frequently encountered in the pyrimidine series [9].



2-Amino-6-hydroxy-4,5-diaminopyrimidine does not enter into the O. Hinsberg reaction [8] under the usual conditions of the experiment; the reaction of this diamine with selenium dioxide gave a substance devoid of selenium, which was not investigated further. 4,6-Dichloropyrimido-2,1,3-selenadiazole (VIII), as the experimental data revealed, is characterized by a high reactivity; the chlorine atoms are cleaved even when the compound is heated moderately in the common solvents; in view of this, compound (VIII) could not be isolated in the pure state. The mobility of the chlorine atoms in (VIII) is apparently of the same order as in the chloro derivatives of the purine series [10]; consequently, (VIII) was identified as 4,6-bis(diethanolamino)pyrimido-2,1,3-selenadiazole (XI), obtained by reacting (VIII) with diethanolamine.



EXPERIMENTAL

4,6-Dioxo-5,7-dimethylpyrimido-2,1,3-selenadiazole (VI). A solution of 1.3 g of selenium dioxide in 5-7 ml of water was added gradually to a solution of 1.5 g of 1,3-dimethyl-4,5-diaminouracil in 20 ml of dilute acetic acid (1 : 3). In measure with adding the former, the color of the reaction mass changed from originally yellow to red, and then to violet. After 2 hr the precipitate was filtered, washed with water, and dried. We obtained 1.4 g of red crystals, which, after recrystallization from water or from 50% alcohol, melted at 230-231°. The selenium was determined quantitatively by mineralizing the substance with nitric acid (d 1.52) and subsequent iodometric titration of the formed selenium dioxide. Approximately 0.5 g of the substance was boiled with 10 ml of nitric acid, and after dilution with water (to 100 ml), followed by the addition of 20 ml of hydrochloric acid (d 1.19) and 0.5 g of potassium iodide, the liberated iodine was titrated with 0.02 N thiosulfate solution in the presence of chloroform; a blank experiment was run at the same time (1 ml of 0.02 N thiosulfate solution corresponds to 0.0003168 g of selenium).

Found %: N 22.49, 22.88; Se 32.15, 32.12. C₆H₆O₂N₄Se. Calculated %: N 22.84; Se 32.23.

4,6-Dioxo-7-methylpyrimido-2,1,3-selenadiazole (VII). A solution of 1.5 g of selenium dioxide in 5 ml of water was added to a solution of 1.5 g of 3-methyl-4,5-diaminouracil in 20 ml of dilute acetic acid (1 : 3), and the reaction mixture was worked up as described above; we obtained 2.1 g of crystals (93% yield), soluble in acetic acid, which, after recrystallization from 50% alcohol, melted at 308-308.5°.

Found %: N 24.61, 24.13; Se 32.70, 32.90. C₆H₄O₂N₄Se. Calculated %: N 24.24; Se 34.19.

4,6-Dihydroxypyrimido-2,1,3-selenadiazole (V). a) A solution of 3 g of selenium dioxide in 10 ml of water was added to a suspension of 2.5 g of 2,6-dihydroxy-4,5-diaminopyrimidine sulfate in 20 ml of hot water and the mixture was heated on the boiling water bath for 2 hr; after cooling, the precipitate was filtered, washed with water, and dried. We obtained 1.9 g (50%) of a pale yellow powder, which could be recrystallized from either water or acetic acid, and which did not melt when heated to 330°.

Found %: N 25.73, 25.80; Se 36.80, 36.36. $C_4H_2O_2N_4Se$. Calculated %: N 25.8; Se 26.45.

b) A solution of 3 g of selenium dioxide in 10 ml of water was added to a suspension of 2.5 g of 2-mercapto-6-hydroxy-4,5-diaminopyrimidine in 20 ml of hot water and the mixture was treated in the same manner as described above. We obtained 1.5 g (42%) of a brownish powder, which after recrystallization from dilute hydrochloric acid did not melt when heated to 330°, and which, based on the elemental analysis data, corresponded to the above described material.

Found %: N 25.86, 25.93; Se 36.40, 34.90. $C_4H_2O_2N_4Se$. Calculated %: N 25.80; Se 36.45. $C_4H_2ON_4SSe$. Calculated %: N 24.03; Se 33.90.

In order to identify it, the substance was methylated; 0.25 g of the substance was mixed with 4 ml of water, after which 0.5 ml of 36% NaOH solution and 0.8 ml of dimethyl sulfate were added to this suspension in 1 hr; the obtained precipitate was filtered and then recrystallized from 50% alcohol. The mixed melting point with authentic 4,6-dihydroxy-5,7-dimethylpyrimido-2,1,3-selenadiazole, obtained from 1,3-dimethyl-4,5-diaminouracil and selenium dioxide, was not depressed.

4,6-Dichloropyrimido-2,1,3-selenadiazole (VIII). A saturated solution of selenium dioxide in acetic acid was added gradually to a suspension of 1 g of 2,6-dichloro-4,5-diaminopyrimidine (IV) in 30 ml of acetic anhydride. After 1 hr the precipitate was filtered and dried. We obtained 0.9 g of substance, which, because of its easy decomposition, was identified by its reaction with diethanolamine.

4,6-Bis(diethanolamino)pyrimido-2,1,3-selenadiazole (XI). A mixture of 0.6 g of (VIII), 10 ml of alcohol and 1.6 g of diethanolamine was heated under reflux for 1 hr, after which the reaction mass was concentrated to a sirup by heating on the water bath; after cooling, the residue was boiled with water in the presence of carbon and filtered hot. The filtrate on cooling deposited yellow crystals, which were filtered and washed with cold water. We obtained 0.9 g of substance, which, after recrystallization from water, melted at 114.5-116°.

Found %: N 21.58, 20.83; Se 20.20, 20.21. $C_{12}H_{20}O_4N_6Se$. Calculated %: N 21.48; Se 20.20.

The intermediates, needed to carry out the described syntheses, i.e., 2,6-dihydroxy-4-aminopyrimidine, 5-nitro-2,6-dihydroxy-4-aminopyrimidine, 2,6-dichloro-5-nitro-4-aminopyrimidine and 2,6-dichloro-4,5-diaminopyrimidine, were synthesized by procedures described in the literature [11, 12].

SUMMARY

1. The reaction of 2,6-dihydroxy-, 2,6-dihydroxy-1,3-dimethyl- and 2,6-dihydroxy-3-methyl-4,5-diaminopyrimidines with selenium dioxide gave the corresponding pyrimido-2,1,3-selenadiazole derivatives; 2-amino-6-hydroxy-4,5-diaminopyrimidine does not react with selenium dioxide under the given conditions.

2. The reaction of 2,6-dichloro-4,5-diaminopyrimidine with selenium dioxide supposedly gave 4,6-dichloropyrimido-2,1,3-selenadiazole, which when reacted with diethanolamine was converted (supposedly) to 4,6-bis(diethanolamino)pyrimido-2,1,3-selenadiazole.

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SYNTHESIS AND STUDY OF SOME 5,5-DIALKYL-AMINOALKYL DERIVATIVES OF BARBITURIC AND THIOBARBITURIC ACIDS

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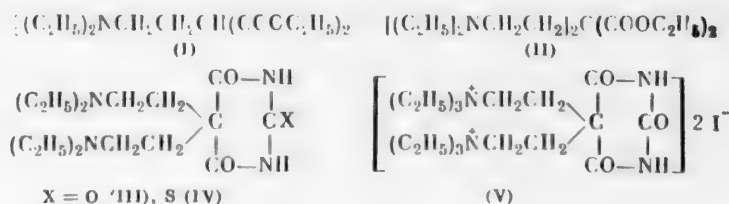
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In order to study the relationship between chemical structure and biological activity we synthesized the previously unknown 5,5-dialkylaminoethyl derivatives of barbituric and thiobarbituric acids.

Starting with malonic ester and diethylaminoethyl chloride, in the presence of sodium ethylate, we synthesized the diethyl ester of (diethylaminoethyl)malonic acid (I), and then the diethyl ester of bis(diethylaminoethyl)malonic acid (II), which was condensed with urea, and also with thiourea, in the presence of sodium ethylate, where we isolated the corresponding barbiturates (III and IV) and the dihydrochloride of 5,5-bis(diethylaminoethyl)barbituric acid. The reaction of (III) with ethyl iodide gave the quaternary ammonium base (V).



It should be mentioned that the direct synthesis of C₂-disubstituted malonic ester containing the diethylaminoethyl radical proceeds in low yield (not exceeding 10%), and consequently we first prepared the mono derivative, which was then converted to the disubstituted malonic ester.

In contrast to the numerous other barbituric acid derivatives described in the literature [1], the synthesized barbiturates are readily soluble in water, as are also the quaternary salts obtained by reacting the barbiturates with ethyl iodide, which facilitated their biological testing.

Pharmacological testing of the compounds, done under the supervision of Prof. V. M. Karasik, revealed that both the barbiturates and their quaternary salts are completely nontoxic and do not exhibit either soporific, or anesthetic, or ganglion-blocking action; we take this opportunity to express our thanks for the performed biological testing.

EXPERIMENTAL

Diethyl ester of (diethylaminoethyl)malonic acid (I). To the sodium ethylate, prepared from 2.3 g of metallic sodium and 60 ml of anhydrous alcohol, was added 16 g of diethyl malonate with stirring, and after distilling off the alcohol at 30° (20 mm), a 50% benzene solution containing 0.1 g-mole of diethylaminoethyl chloride was added in 30 min. Then the reaction mixture was heated for 9 hr on the boiling water bath with constant stirring. After cooling, the solution was treated with 100 ml of water and the reaction product was extracted from the aqueous solution with chloroform. After distilling off the chloroform, the residue was subjected to fractional distillation. We obtained 13 g of compound with b.p. 134-142° (12 mm), and n_D^{20} 1.4383.

Diethyl ester of bis(diethylaminoethyl)malonic acid (II). Into a three-necked flask, fitted with a mechanical stirrer, a reflux condenser with a calcium chloride tube, and a dropping funnel, was charged 60 ml of anhydrous al-

cohol, followed by the gradual addition of 1.67 g of metallic sodium and 19 g of the diethyl ester of (diethylaminoethyl)malonic acid (b.p. 134-142°/12 mm). After this the alcohol was distilled off and a solution of 11 g of diethylaminoethyl chloride in xylene was added from the dropping funnel. The mixture was heated in an oil bath at 110° for 10 hr with constant stirring. The mixture after cooling was filtered and the filtrate was treated with 50 ml of water, after which the xylene layer was separated and dried over fused sodium sulfate. After distilling off the solvent, the residue was distilled to give 13 g (50%) of a fraction with b.p. 155-156° (2.5 mm), and n_D^{20} 1.4543.

Found %: N 7.99, 8.18. $C_{19}H_{38}O_4N_2$. Calculated %: N 7.82.

Dihydrochloride of 5,5-bis(diethylaminoethyl)barbituric acid. To 6 g of urea, dried at 80°, were added 80 ml of anhydrous alcohol and 35.8 g of the diethyl ester of bis(diethylaminoethyl)malonic acid (b.p. 155-156° at 2.5 mm). After distilling off the alcohol in vacuo, the residue was dissolved in 100 ml of water and the unreacted disubstituted malonic ester was extracted with ether; the water layer was acidified with hydrochloric acid until acid to Congo, but after concentrating on the boiling water bath to a sirupy mass and dissolving in alcohol, nothing but sodium chloride was isolated. The filtrate after evaporation in vacuo was a brown amorphous mass, avidly absorbing moisture from the air; after recrystallization from alcohol a substance with m.p. 148-150° was isolated.

Found %: N 13.46, 13.93. $C_{16}H_{32}O_3N_4Cl_2$. Calculated %: N 14.04.

Picrate of 5,5-bis(diethylaminoethyl)barbituric acid. A solution of 0.9 g of picric acid in 10 ml of alcohol, obtained by heating, was added to a solution of 0.5 g of the dihydrochloride of 5,5-bis(diethylaminoethyl)barbituric acid in 10 ml of alcohol; the obtained bright yellow, finely divided precipitate was filtered, washed with water, and recrystallized from alcohol. M.p. 219-220°.

Found %: N 17.86, 18.06. $C_{22}H_{33}O_{10}N_7$. Calculated %: N 17.66.

5,5-Bis(diethylaminoethyl)barbituric acid (III). A solution of 5 g of the dihydrochloride of 5,5-bis(diethylaminoethyl)barbituric acid in 10 ml of water was cooled to 0° and then neutralized with 25% NaOH solution; the obtained long colorless needles were filtered, and after recrystallization from benzene the compound melted at 138-139°.

Found %: N 17.11, 17.44. $C_{16}H_{30}O_3N_4$. Calculated %: N 17.18.

Barbituric acid, 5,5-bis(triethylaminoethyl iodide) (V). To 2 g of the dihydrochloride of 5,5-bis(diethylaminoethyl)barbituric acid in 10 ml of anhydrous alcohol was added 2 ml of ethyl iodide and the mixture was heated on the boiling water bath for 2 hr. On cooling, a voluminous white precipitate was obtained, which after recrystallization from alcohol melted at 217-219°.

Found %: N 8.69, 8.98. $C_{20}H_{40}O_3N_4I_2$. Calculated %: N 8.78.

5,5-Bis(diethylaminoethyl)thiobarbituric acid (IV). To 7.6 g of thiourea, dried at 80°, in the presence of sodium ethylate, was added 35.8 g of the diethyl ester of bis(diethylaminoethyl)malonic acid, after which the reaction mixture was heated for 14 hr at 80-90°. Then the solvent was removed by vacuum-distillation, and the reaction product was dissolved in water and acidified with hydrochloric acid (d 1.04) to pH 8. Here a yellow amorphous precipitate was obtained, which after recrystallization from benzene melted at 168-169°. Yield 25%.

Found %: N 16.11, 16.42; S 8.74, 8.61. $C_{16}H_{30}O_2N_4S$. Calculated %: N 16.37.

SUMMARY

Derivatives of barbituric and thiobarbituric acids, containing diethylaminoethyl radicals on C_5 , were synthesized by reacting the disubstituted malonic ester with urea and thiourea.

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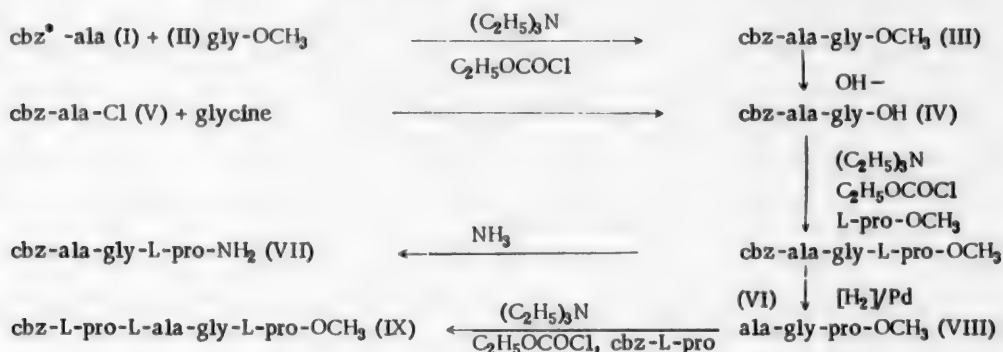
SYNTHESIS OF THE COLLAGENASE SUBSTRATE - METHYL ESTER OF CARBOBENZOXY-L-PROLYL-L- ALANYLGLYCYL-L-PROLINE

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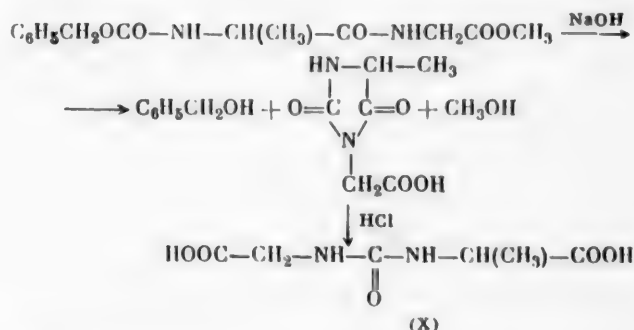
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The enzyme, collagenase from *Clostridium histolyticum*, recently characterized in a number of laboratories [1], and its other closely related varieties, have attracted the attention of investigators because of their unusually narrow proteolytic specificity. After some unsuccessful attempts to obtain synthetic substrates for this enzyme [2], the searches finally led to success. At almost the same time communications appeared from four different laboratories on the obtaining of synthetic substrates for the enzyme [3].

The synthesis of two collagenase substrates, composed of glycine, L-proline and alanine, is described in the present paper. In this connection the substrates were obtained using both D,L-alanine and L-alanine. The methyl ester of carbobenzoxy-L-prolyl-D,L-alanylglycyl-L-proline and the methyl ester of carbobenzoxy-L-prolyl-L-alanylglycyl-L-proline were synthesized by the following scheme.



When the methyl ester of carbobenzoxy-D,L-alanylglycine was saponified with 2 N NaOH, using the procedure described in the literature [4], we observed, together with the main process of saponification of the ester group and the formation of carbobenzoxy-D,L-alanylglycine, also the formation of the urea derivative, N-carboxymethyl-N'-methylcarboxymethylurea, in 33% yield. It is probable that the reaction investigated by Maclaren [5] takes place here.



* L-Alanine and D,L-alanine; cbz = C₆H₅CH₂OCO-.

Compound (X) was characterized by analysis; in addition, its infrared spectrum is different from that of carbobenzoxy-D,L-alanylglycine (IV), and it also depresses the melting point when mixed with carbobenzoxyalanylglycine (IV). The infrared spectrum of carbobenzoxyalanylglycine displayed a number of bands, characteristic for the C = C linkage in aromatic systems, and specifically, bands showing maximum absorption at 1520 and 1560 cm^{-1} , whereas the spectrum of (X) contains only one band in the interval 1700-1417 cm^{-1} with a maximum at 1530 cm^{-1} , which indicates that the benzene structure is absent in compound (X).

Carbobenzoxy-D,L-alanylglycine (IV) was synthesized by two procedures - via the acid chloride of carbobenzoxyalanine (V) by the Fischer method, and by saponifying the methyl ester of carbobenzoxy-D,L-alanylglycine (III). The latter was synthesized by the technique of mixed anhydrides using ethyl chloroformate. The specific rotations of the products obtained by the two methods were compared; here it proved that the method of mixed anhydrides in chloroform gives greater racemization than does the acid chloride method; however, the latter method is also not free of racemization.

An interesting fact that should be mentioned is that when studying the substrate activity of the final and intermediate products we found that the amide of carbobenzoxyalanylglycylproline (VII) is attacked by collagenase, while the methyl ester of carbobenzoxyalanylglycylproline (VI) fails to suffer cleavage, whereas both the amide and the methyl ester of carbobenzoxyprolylalanylglycylproline (IX) are cleaved to the same degree by collagenase.

EXPERIMENTAL

Methyl ester of carbobenzoxy-D,L-alanylglycine (III). Six grams of carbobenzoxyalanine was dissolved in 15 ml of chloroform, containing 3.8 ml of triethylamine. The solution was cooled to -15° and then mixed at this temperature with 2.5 ml of ethyl chloroformate. The reaction mixture was kept at -3 to -5° for 15-20 min, again cooled to -15° , and then mixed with a previously cooled chloroform solution, containing 3.38 g of the hydrochloride of methyl glycinate and 3.8 ml of triethylamine. The reaction mixture was then kept for 2 hr at 0° and for 12 hr at room temperature. The chloroform layer was washed with water, 1 N HCl, twice with 0.5 N Na_2CO_3 , and again with water, after which it was dried over Na_2SO_4 . After distilling off the solvent we obtained 4.4 g (57%) of an oil, which crystallized when petroleum ether was added. M.p. $62-65^\circ$ (from water).

Found %: C 57.48, 57.51; H 6.21, 6.10. $\text{C}_{14}\text{H}_{18}\text{O}_5\text{N}_2$. Calculated %: C 57.25; H 6.15.

Carbobenzoxy-D,L-alanylglycine (IV). A solution of 2.5 g of the methyl ester of carbobenzoxy-D,L-alanylglycine [6] in 7.5 ml of acetone was mixed with 6.5 ml of 2 N NaOH and the ester was saponified by keeping the reaction mixture at room temperature for 2 hr. Then the reaction mixture was acidified until distinctly acid to Congo red and evaporated to dryness. The residue was extracted 3 times with hot chloroform. The chloroform extract was evaporated to a volume of 10-15 ml and the substance was made to crystallize by the addition of 20-30 ml of ether. Yield 1.5 g (63%), m.p. 132° (from water).

N-Carboxymethyl-N'-methylcarboxymethylurea (X). One gram of the methyl ester of carbobenzoxy-D,L-alanylglycine (III) was saponified at about 20° with 6 ml of 2 N NaOH. The substance quickly dissolved in the alkali, forming a clear solution. Within 30 min the solution turned cloudy, followed by the formation of a white emulsion, and finally, after 2 hr, an organic layer separated, smelling strongly of benzyl alcohol. The alkaline solution was washed with ether, and the ether layer was discarded. The aqueous fraction was acidified until acid to Congo red and then was placed in the refrigerator for a day. The obtained crystals were filtered. We obtained 320 mg of (X) with m.p. $138-139^\circ$. The substance was recrystallized from 1.5 ml of water, m.p. 142° . The mixed melting point with carbobenzoxy-D,L-alanylglycine was $125-130^\circ$.

Found %: C 39.15, 39.45; H 5.14, 5.31. $\text{C}_6\text{H}_{10}\text{O}_5\text{N}_2$. Calculated %: C 37.95; H 5.25.

The filtrate after the removal of (X) was evaporated in vacuo to dryness, and the residue was extracted 3 times with hot chloroform. The chloroform was evaporated in vacuo, and the residual oil was made to crystallize by dissolving in chloroform and then adding ether; m.p. 131° . The yield of carbobenzoxy-D,L-alanylglycine (IV) was 380 mg (40%).

Amide of carbobenzoxy-D,L-alanylglycyl-L-proline (VII). Starting with 2.16 g of carbobenzoxyalanylglycine (IV) and 0.9 g of the methyl ester of proline (b.p. 60.5° at 9 mm), the methyl ester of carbobenzoxy-D,L-alanylglycylproline (VI) was obtained by the usual technique of preparing mixed anhydrides using ethyl chloroformate. The yield of the yellow oil was 3.01 g (94.2%). The substance was dissolved in methanol and decolorized by boiling with animal charcoal. The obtained colorless oil was used in subsequent syntheses.

A solution of 497 mg of the methyl ester of carbobenzoxy-D,L-alanylglycyl-L-proline (VI) in 15 ml of anhydrous methanol was saturated at 0° with dry ammonia. The solution was then kept at 20° for 2 days. The methanol was vacuum-distilled. The residue was dissolved in 2 ml of methanol and then precipitated by the addition of ether. The yield of white powder was 140 mg (29%), m.p. 182-184°.

Found %: C 56.94, 56.99; H 6.42, 6.22. $C_{18}H_{24}O_5N_4$. Calculated %: C 57.47; H 6.70.

Methyl ester of carbobenzoxy-L-prolyl-D,L-alanylglycyl-L-proline (IX). One gram of the methyl ester of carbobenzoxy-D,L-alanylglycylproline (VI) was dissolved in 25 ml of methanol and then hydrogenated over Pd-black. After distilling off the solvent we obtained 505 mg of the methyl ester of D,L-alanylglycylproline (VIII) as an oil, which was used as such in subsequent synthesis. Starting with 754 mg of carbobenzoxy-L-proline and 785 mg of the methyl ester of D,L-alanylglycylproline (VII) we obtained, using the usual technique for preparing mixed anhydrides, 1.4 g (95%) of an oil, which crystallized when ether was added. The substance (IX) was reprecipitated from chloroform solution with ether. M.p. 135-150°, $[\alpha]_D^{25} - 95^\circ$ (c 1, methanol).

Found %: C 58.50, 58.50; H 6.69, 6.57; N 11.34, 11.16. $C_{24}H_{30}O_7N_4$. Calculated %: C 58.98; H 6.50; N 11.52.

Methyl ester of carbobenzoxy-L-alanylglycine (III). Starting with 2.8 g of carbobenzoxy-L-alanine (m.p. 85°) and 1.59 g of the hydrochloride of methyl glycinate, the compound was obtained in the same manner as the methyl ester of carbobenzoxy-D,L-alanylglycine, employing the usual technique for the preparation of mixed anhydrides. The yield of colorless oil, which was recrystallized from a mixture of ethyl and petroleum ethers, was 2.93 g, m.p. 94-96°, $[\alpha]_D^{21} - 25^\circ$ (c 5, methanol).

Found %: C 57.12, 57.10; H 6.07, 6.23. $C_{14}H_{18}O_5N_2$. Calculated %: C 57.25; H 6.15.

Acid chloride of carbobenzoxy-L-alanine (V). The compound was obtained by the method previously described by us for the preparation of the acid chloride of carbobenzoxyglycine [6]. A solution of 1 g of carbobenzoxy-L-alanine in 15 ml of absolute ether was treated at 0° with 1 g of PCl_5 . The reaction mixture was shaken at 0° for about an hour until nearly all of the PCl_5 had dissolved. The solution was filtered rapidly using slight cooling. The clear solution was then poured into 250 ml of petroleum ether, cooled to -40°. The obtained needles of (V) were filtered, m.p. 37-38°. Yield 840 mg.

Carbobenzoxy-L-alanylglycine. Method A. To a solution of 300 mg of glycine in 2.5 ml of 2 N NaOH at 0° was added, with stirring, 840 mg of freshly prepared carbobenzoxy-L-alanyl chloride (V) in 30-40 min. After all of the added acid chloride had dissolved, the solution was kept for another 15 min at 0°, after which it was filtered, and the filtrate was acidified with 6 N HCl until acid to Congo. The obtained oil was extracted with ethyl acetate. The extract was dried over Na_2SO_4 , followed by evaporation of the solution in vacuo to a volume of 2.5 ml, and treatment of the residue with ether to precipitate the substance. We obtained 253 mg of (IV), m.p. 124-128°, $[\alpha]_D^{23} - 16.3^\circ$ (c 3, methanol).

Found %: C 55.86, 55.78; H 5.98, 6.05. $C_{13}H_{16}O_5N_2$. Calculated %: C 55.8; H 5.72.

Method B. A solution of 5 g of the methyl ester of carbobenzoxy-L-alanylglycine (III) in 20 ml of acetone was saponified by treatment with NaOH solution at room temperature (21-22°) for 2 hr. The solution was then acidified to Congo red, the acetone was distilled off, and the carbobenzoxy-L-alanylglycine (IV) was extracted with ethyl acetate. The ethyl acetate solution was extracted with $KHCO_3$ solution, and after acidification of the latter, the substance was again extracted with ethyl acetate. The ethyl acetate layer was washed with dilute hydrochloric acid, and then with water. After drying the solution over Na_2SO_4 , the solvent was removed by distillation. The residue was recrystallized from a mixture of ethyl acetate and petroleum ether, m.p. 120-125°. The yield of (IV) was 2.66 g (55%), $[\alpha]_D^{23} - 14.2^\circ$ (c 3, methanol).

Found %: C 55.74, 55.68; H 5.89, 5.91. $C_{13}H_{16}O_5N_2$. Calculated %: C 55.8; H 5.72.

Methyl ester of carbobenzoxy-L-prolyl-L-alanylglycyl-L-proline (IX). Obtained in the same manner as the methyl ester of carbobenzoxy-L-prolyl-D,L-alanylglycyl-L-proline. From 2 g of carbobenzoxy-L-alanylglycine and 0.7 g of the methyl ester of proline we obtained the methyl ester of carbobenzoxy-L-alanylglycyl-L-proline (VI) in 90% yield. The compound, a yellow oil, was dissolved in methanol and decolorized with animal charcoal. The thus obtained colorless oil was used as such in subsequent syntheses.

A solution of 760 mg of the methyl ester of carbobenzoxy-L-alanylglycyl-L-proline (VI) in 15 ml of methanol, containing 3 drops of water and 3 drops of glacial acetic acid, was hydrogenated over Pd-black for 2 hr at room tem-

perature, until the theoretical amount of hydrogen was absorbed. Then the catalyst was filtered and the solvent was removed by evaporation. We obtained 425 mg (85% yield) of the methyl ester of L-alanylglycyl-L-proline (VIII), which was used as such in subsequent synthesis. The chromatogram of the substance gave one stain with $R_f = 0.57$ (butanol-water- $\text{CH}_3\text{COOH} = 4 : 5 : 1$).

Analogous to the methyl ester of carbobenzoxy-L-prolyl-L-alanylglycyl-L-proline, from 425 mg of the methyl ester of L-alanylglycyl-L-proline (VIII) and 266 mg of carbobenzoxy-L-proline we obtained 830 mg (89%) of the methyl ester of carbobenzoxy-L-prolyl-L-alanylglycyl-L-proline (IX). After recrystallization from ether, m.p. 136-143°, $[\alpha]_D^{22} = 119^\circ$ (c 1, methanol).

Found %: C 58.48, 58.64; H 6.55, 6.48; N 11.44, 11.85. $\text{C}_{24}\text{H}_{30}\text{O}_7\text{N}_4$. Calculated %: C 58.98; H 6.50; N 11.52.

SUMMARY

1. The synthesis of the collagenase substrate, the methyl ester of carbobenzoxy-L-prolyl-L-alanylglycyl-L-proline, was described.
2. It was shown that N-carboxymethyl-N'-methylcarboxymethylurea is formed as a by-product in the saponification of the methyl ester of carbobenzoxy-L-alanylglycine.

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TIN AND LEAD ORGANIC DERIVATIVES OF NICOTINIC ACID

D. A. Kochkin and I. B. Chekmareva

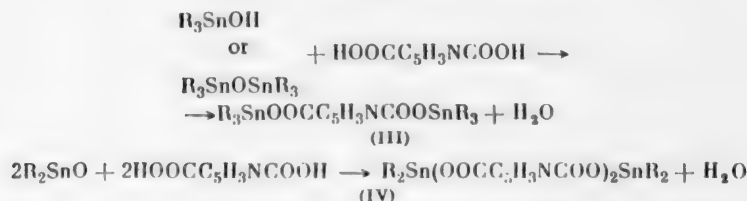
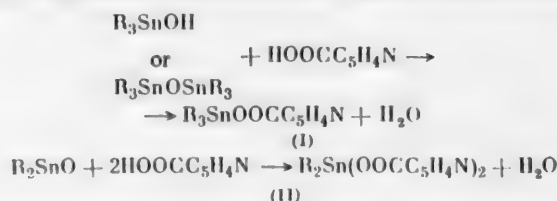
All-Union Vitamin Research Institute

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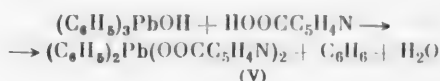
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Original article submitted August 8, 1960

In the present work we describe the synthesis and properties of tin and lead organic derivatives of nicotinic acid. We have obtained trialkylstannyl (I) and dialkylstannyl (II) esters of nicotinic acid, and trialkylstannyl (III) and dialkylstannyl (IV) esters of 2,5-pyridine dicarboxylic acid (isocinchomeric acid),



In preparing the lead organic derivatives of nicotinic acid we have found an interesting rearrangement of hydroxyl-containing lead organic compounds connected with splitting of the phenyl group and formation of a diphenyl lead ester of the acid. Such a split was previously established in the reaction of triphenylplumbanol with methacrylic acid [2].



The compounds which we synthesized are crystalline substances soluble in chloroform, benzene, alcohols, and other organic solvents; insoluble or soluble with difficulty in water. Some of the physicochemical properties of the synthesized compounds are given in the table.

EXPERIMENTAL

1. Tri-n-propylstannyl ester of nicotinic acid. In a three-necked flask fitted with a stirrer and dropping funnel we placed 1.2 g (0.01 mole) of nicotinic acid and 30 ml of water. After heating the mixture and dissolving the acid we added 2.6 g (0.05 mole) of hexa-n-propylstannoxide, b.p. 148° (3 mm), n_D^{20} 1.4315, d_4^{20} 1.2514 [1]. The reaction mixture was heated to 70° for one hour. An oily liquid formed and quickly solidified into a crystalline mass. The crystals were filtered off on a glass filter, washed several times with hot water, and dried in a vacuum desiccator. Yield 2.9 g (80%). M.p. 90-92° (from benzene). The trialkylstannyl esters of nicotinic acid were synthesized in an analogous way from the trialkylstannols.

2. Diethylstannyl ester of nicotinic acid. We placed in a three-necked flask 2.2 g (0.01 mole) of diethylstannone (obtained by hydrolysis of diethyldichlorostannane [1]), 20 ml of water, and 2.7 g (0.022 mole) of nicotinic acid. The reaction mixture was heated to boiling for 20 minutes. At first the products dissolved, and then a crystal-

Compound	M.p.	Yield, %	Found, %			Calculated, %		
			C	H	N	C	H	N
(I), R=CH ₃	188-190°	82.3	37.72, 38.07	4.70, 4.81	5.17, 5.19	37.81	4.58	4.89
(II), R=C ₂ H ₅	108-110	85.6	43.91, 43.67	5.95, 5.90	4.64, 4.43	43.93	5.93	4.27
(III), R=C ₃ H ₇	90-92	79.3	49.00, 49.15	7.02, 7.04	3.74, 3.60	48.71	6.81	3.71
(IV), R=C ₄ H ₉	211-212	85.7	45.60, 45.09	4.00, 3.94	6.13, 6.34	45.65	4.31	6.65
(V), R=C ₅ H ₁₁	156-158	82.4	47.59, 47.83	4.81, 4.69	6.13, 6.17	48.14	4.94	6.24
(VI), R=C ₆ H ₁₃	263	50.1	39.25, 39.20	5.64, 5.88	2.58, 2.61	39.56	5.76	2.42
(VII), R=C ₇ H ₁₅	144-145	31.3	45.18, 45.00	6.61, 6.85	2.21, 2.21	45.43	6.86	2.12
(VIII), R=C ₈ H ₁₇	300 decomp.	60.3	38.53, 38.43	3.61, 3.72	3.82, 3.86	38.63	3.85	4.09
(IX), R=C ₉ H ₁₉	250 decomp.	59.6	42.21, 42.62	4.31, 4.21	3.62, 3.57	42.21	4.63	3.78
(X), R=C ₁₀ H ₂₁	200 decomp.	71.1	47.76, 47.80	3.07, 3.17	10.52, 10.63	47.59	2.99	10.57

line precipitate began to appear, which was filtered off on a glass filter and washed with 3-4 portions of hot water. Then it was dried to constant weight. M.p. 156-158° (from chloroform). Soluble in chloroform and benzene, not soluble in water.

3. Bis-triethylstannyl ester of 2,5-pyridine dicarboxylic (isocinchomeronic) acid. In a three-necked flask fitted with a stirrer was placed 2.2 g (0.01 mole) of triethylstannol or hexaethylstannoxide [1] and 35 ml of water. After solution, we added 0.8 g of 2,5-pyridine dicarboxylic acid (m.p. 245°) and boiled under reflux to solution of the acid. The crystalline precipitate was filtered off, washed with three portions of hot water, recrystallized from hot chloroform, and dried to constant weight. Yield 1.4 g (50.1%). M.p. 263° (with decomposition).

4. Reaction of dialkylstannones and isocinchomeronic acid. We placed in a flask 1.9 g (0.01 mole) of diethylstannone, 25 ml of water, and 1.6 g of isocinchomeronic acid. The mixture was heated to boiling, boiled for 30 minutes, and left overnight. The crystalline precipitate was washed with several portions of hot water and hot chloroform, and dried in a vacuum desiccator to constant weight. From the analytical data, the crystalline substance was assigned a cyclic structure. It did not dissolve in the ordinary solvents. M.p. above 300° (with decomposition).

5. Diphenyllead ester of nicotinic acid. We placed in a three-necked flask 4.6 g (0.01 mole) of triphenylplumbanol [2] (obtained by hydrolysis of triphenylchloroplumbane with alcoholic alkali) and 20 ml of alcohol. After solution, we added 1.2 g (0.01 mole) of nicotinic acid and heated the reaction mixture to boiling and full solution of the reagents. The mixture was boiled for 1.5 hours on a water bath. At the end of boiling a crystalline precipitate came down which was filtered off, washed with several portions of hot water, and dried to constant weight. Easily soluble in benzene, and chloroform, poorly so in alcohol, insoluble in water.

SUMMARY

1. We have synthesized trialkyl- and dialkyltin esters of nicotinic and 2,5-pyridine dicarboxylic acids.

2. We have obtained the diphenyllead ester of nicotinic acid. We have shown the splitting of triphenylplumbanol with formation of the diphenyllead ester of the acid.

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THE REACTION OF α -HYDROXYACIDS WITH PHOSPHORUS TRICHLORIDE

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and A. I. Roikh

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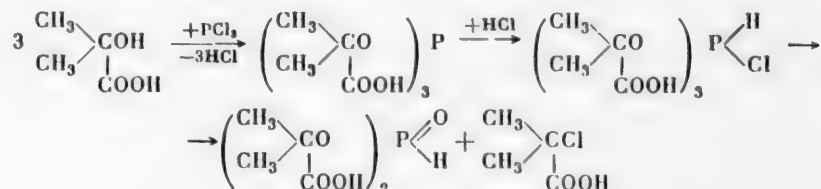
Due to the presence in hydroxyacids of two functional groups, we can expect their reaction with phosphorus trichloride either on the hydroxyl group, on the carboxyl group, or on both groups at once.

Alcohols reacting with phosphorus trichloride in a 1 : 1 molar ratio usually form alkylidichlorophosphites [1]. When three moles of alcohol and one mole of phosphorus trichloride react in the absence of a base, dialkylphosphites are largely formed. The reaction takes place according to the scheme of the Arbuzov rearrangement [2].

Phosphorus trichloride reacts with organic acids in the absence of a base to form exclusively the corresponding acid chloride. The mechanism of this reaction has not been established conclusively enough [3]. It has been found that hydroxyacids of the aromatic series: salicylic [4], 3,5-dichlorosalicylic, 3-chlorosalicylic, 3,5-diiodosalicylic, and methylsalicylic acids [5] react with phosphorus trichloride with formation of compounds with a bicyclic structure. Of the hydroxyacids of the aliphatic series only lactic acid has been studied; with phosphorus trichloride this gives a crystalline product whose structure has not been established [6].

As the objects of the present investigation we have chosen α -hydroxypropionic, α -hydroxybutyric, α -hydroxyisobutyric, α -hydroxyvaleric, α -hydroxyhexanoic, and α -hydroxycyclohexanoic acids. The reaction of these hydroxyacids with phosphorus trichloride is accompanied by strong heating and evolution of hydrogen chloride. However, in most cases the isolation of individual compounds from the reaction products was not successful. Only hydroxyisobutyric and hydroxycyclohexanoic acids gave compounds which were not soluble in phosphorus trichloride, and the isolation of reaction products was therefore easier.

The reaction product from α -hydroxyisobutyric acid and phosphorus trichloride was a colorless substance with m.p. 129° with crystals in the form of quadratic plates. It was very easily hydrolyzed in air, liberating α -hydroxyisobutyric acid. Even when kept in a closed vessel its melting point fell to 120° on the second day and to 106° after several days. Recrystallization from hot carbon tetrachloride could again give a product with m.p. 129°. The compound did not react with phenylazide. Hence the phosphorus in the compound was in the pentavalent state [7]. Its ability to condense with chloral confirmed the presence of the group $\text{>P} \begin{smallmatrix} \text{O} \\ \text{H} \end{smallmatrix}$ [8]. We can assume that the product of the reaction of hydroxyisobutyric acid with phosphorus trichloride is bis- α -carboxyisopropylphosphorous acid, which can be formed as a result of the following reactions.



The results of titration of bis- α -carboxyisopropylphosphorous acid with alkali confirm this scheme. The presence of free carboxyl groups is confirmed by its reaction with phosphorus pentachloride.

EXPERIMENTAL

Reaction of α -hydroxyisobutyric acid with phosphorus trichloride. To 52.0 g of hydroxyisobutyric acid heated to 50° with stirring we added dropwise 46.0 g of phosphorus trichloride. After addition of the whole amount, the mixture was kept for one hour at 85-90°. When cooled to 70°, fine crystals appeared and were filtered off, washed with ether, and recrystallized. Yield 35.0 g (82.6%). M.p. 129° (from hot CCl_4). Easily soluble in dioxane, acetone, and ethanol, and when heated, in carbon tetrachloride and aromatic hydrocarbons; insoluble in ether and hexane. Water easily hydrolyzed them.

Found %: P 12.50, 12.45. M 250. $\text{C}_8\text{H}_{15}\text{O}_7\text{P}$. Calculated %: P 12.20. M 254.

Reaction of α -hydroxycyclohexanoic acid with phosphorus trichloride. To 14.4 g of hydroxycyclohexanoic acid with stirring and heating to 70° was added 9.6 g of phosphorus trichloride. After keeping for one hour at 100°, the mixture was cooled. At 90°, crystals appeared which were filtered off and recrystallized.

Yield 8.8 g (50.3%); fine needles with m.p. 94-95° (from benzene).

Found %: P 8.35, 8.42. $\text{C}_{14}\text{H}_{23}\text{O}_7\text{P}$. Calculated %: P 9.20.

In the reaction of α -hydroxypropionic, α -hydroxybutyric, α -hydroxyvaleric, and α -hydroxyhexanoic acids with phosphorus trichloride liquid homogeneous masses were formed which after removal of volatile materials by heating in a vacuum passed into a glassy state. We could not isolate individual substances.

Condensation of bis- α -carboxyisopropylphosphorous acid with chloral. In 1.17 g of chloral with heating we dissolved 2.0 g of bis- α -carboxyisopropylphosphorous acid. On the next day a complex crystalline mass had formed. We obtained fine, colorless crystals with m.p. 72° (from ether).

Found %: P 6.30, 6.15. $\text{C}_{11}\text{H}_{16}\text{O}_8\text{PCl}_3$. Calculated %: P 6.20.

Reaction of bis- α -carboxyisopropylphosphorous acid with phenylazide. To 2 g of bis- α -carboxyisopropylphosphorous acid in benzene we added 1 ml of phenylazide. Evolution of nitrogen did not occur even when the solvent was heated to boiling.

Reaction of bis- α -carboxyisopropylphosphorous acid with phosphorus pentachloride. We heated 5.0 g of bis- α -carboxyisopropylphosphorous acid and 5.0 g of phosphorus pentachloride to boiling in 15 ml of phosphorus oxychloride for 30 hours. Energetic evolution of hydrogen chloride occurred. After removal of phosphorus oxychloride in a vacuum, a thick mass remained which partly crystallized after some time. The crystals were washed with ether. We obtained a white crystalline mass which immediately deliquesced in air. It had the characteristic odor of an acid chloride.

SUMMARY

It is shown that the reaction of α -hydroxyisobutyric acid and α -hydroxycyclohexanoic acid with phosphorus trichloride in the absence of a base proceeds with formation of the corresponding bis- α -carboxyalkylphosphorous acid.

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THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO 1,6-HEXAMETHYLENE DIISOCYANATE

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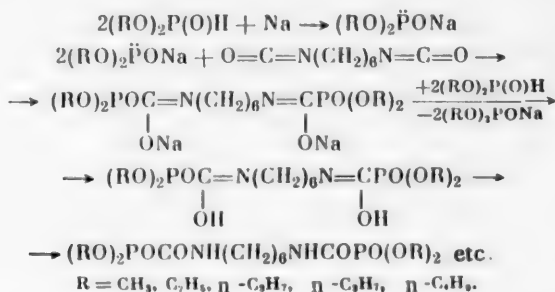
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It is known that dialkylphosphorous acids react easily with esters of isocyanic acid and give substituted amides of dialkylcarbamoylphosphonic acids [1].



It was interesting to carry out the addition of dialkylphosphorous acids to diisocyanates (1,6-hexamethylene diisocyanate). It was shown that the reaction occurs in the presence of alcoholates of the alkali metals or in the presence of alkali metals.



Evidently the metallic sodium by exchange reaction with the dialkylphosphorous acid forms a salt of the dialkylphosphorous acid. Then, due to the unshared electron pair on the phosphorus atom, there is addition of the sodium dialkylphosphorite to the carbonyl groups of the diisocyanate molecule, after which the addition product rearranged into the substituted amide, hexamethylene-1,6-bisdialkyl esters of amidocarbamoylphosphonic acid.

We obtained in pure form and sufficiently good yield the hexamethylene-1,6-bisdimethyl, diethyl, and diisopropyl esters of amidocarbamoylphosphonic acid. The ability to crystallize of the higher esters was less and they crystallized very slowly. Hexamethylene-1,6-bis-di-n-butyl ester of amidocarbamoylphosphonic acid could not be isolated in crystalline form. Hexamethylene-1,6-bis-di-n-propyl and diisobutyl esters crystallized only after standing for 3-6 months. The esters are easily soluble in alcohol, ether, benzene, dioxane, and carbon tetrachloride; white, crystalline substances (see table).

To show the structure of these esters, one of them, hexamethylene-1,6-bisdiisopropyl ester of amidocarbamoylphosphonic acid was prepared by a counter synthesis by the method of A. E. Arbuzov. A mixed sample gave no melting point depression.

We also studied the addition of some substituted dialkylphosphorous acids to 1,6-hexamethylene diisocyanate. We showed that the introduction of the cyano group into the molecule of dialkylphosphorous acid decreased the ability of the latter to undergo the addition reaction, which can be explained by the effect of the cyano group on the mobility of the electron on the phosphorus atom. 1,6-Hexamethylene diisocyanate and α -dicyanoisopropylphosphorous acid were sealed in an ampule and stood for two years. In the first year we noted a small increase in viscosity. β,β' -Dichlorodiethylphosphorous acid under the same conditions reacted faster with 1,6-hexamethylene diisocyanate than

Formula	M.p.	% P		Yield, %
		Found	Calc.	
$(\text{CH}_2)_6 \begin{cases} \text{NHCOPO}(\text{OCH}_3)_2 \\ \text{NHCOPO}(\text{OCH}_3)_2 \end{cases}$	88°	15.22, 15.56	15.8	85
$(\text{CH}_2)_6 \begin{cases} \text{NHCOPO}(\text{OC}_2\text{H}_5)_2 \\ \text{NHCOPO}(\text{OC}_2\text{H}_5)_2 \end{cases}$	54	13.54, 13.7	13.96	82
$(\text{CH}_2)_6 \begin{cases} \text{NHCOPO}(\text{OC}_3\text{H}_7\text{-n})_2 \\ \text{NHCOPO}(\text{OC}_3\text{H}_7\text{-n})_2 \end{cases}$	38	12.24, 12.39	12.4	87
$(\text{CH}_2)_6 \begin{cases} \text{NHCOPO}(\text{OC}_3\text{H}_7\text{-iso})_2 \\ \text{NHCOPO}(\text{OC}_3\text{H}_7\text{-iso})_2 \end{cases}$	102	12.2, 12.3	12.4	84
$(\text{CH}_2)_6 \begin{cases} \text{NHCOPO}(\text{OC}_4\text{H}_9\text{-iso})_2 \\ \text{NHCOPO}(\text{OC}_4\text{H}_9\text{-iso})_2 \end{cases}$	—	10.63, 10.87	11.1	80

did α -dicyanoisopropylphosphorous acid. The more rapid increase in viscosity of the reaction mass in this case showed that the chlorine atom has less effect than the cyanide on the mobility of the electron on the phosphorus atom.

EXPERIMENTAL

Addition of dimethylphosphorous acid to 1,6-hexamethylene diisocyanate. We placed in an ampule 11 g (0.1 mole) of dimethyl phosphorous acid and added small pieces of metallic sodium. Then we introduced 8.4 g (0.05 mole) of 1,6-hexamethylene diisocyanate. The ampule was sealed and allowed to stand at room temperature for ten hours. The reaction was accompanied by heat and increase in viscosity of the reaction mass. After 12 hours, the whole reaction mass crystallized. The ampule was opened and the product was recrystallized. Yield 16.5 g (85%). M.p. 88° (from CCl_4).

Found %: P 15.22, 15.56. $\text{C}_{22}\text{H}_{26}\text{O}_8\text{N}_2\text{P}_2$. Calculated %: P 15.8.

Addition of the other dialkylphosphorous acids to 1,6-hexamethylene diisocyanate was carried out in an analogous manner.

Hexamethylene-1,6-bis-diisopropyl ester of amidocarbamoylphosphonic acid. In a small round bottomed flask fitted with a reflux condenser and calcium chloride tube we placed 8.32 g of triisopropyl phosphite and 4.82 g of hexamethylene-1,6-bishydrochloride of carbamic acid. The reaction was accompanied by slight heating and evolution of isopropyl chloride. Yield 5 g. M.p. 102-103°. A sample mixed with the product obtained by addition of diisopropylphosphorous acid to 1,6-hexamethylene diisocyanate gave no melting point depression.

SUMMARY

1. We have found that dialkylphosphorous acids add to 1,6-hexamethylene diisocyanate with formation of hexamethylene-1,6-bisdialkyl esters of amidocarbamoylphosphonic acid.

We have carried out the addition of dimethyl, diethyl, di-n-propyl, diisopropyl and diisobutylphosphorous acids to 1,6-hexamethylene diisocyanate.

2. The structure of the resulting substances has been shown by a counter synthesis by the method of A. E. Arbuzov.

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THE EFFECT OF CATALYSTS AND PERIOD OF ILLUMINATION
ON THE PHOTOSYNTHESIS OF AMINO ACIDS IN A MIXTURE
OF PARA-FORMALDEHYDE AND POTASSIUM NITRATE

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The formation of amino acids on the surface of the earth is the source of the origin of life on the earth. After the formation of amino acids, the synthesis of peptides and proteins begins, and with the help of these the synthesis of protoplasm is carried out.

Oparin [1] considers that in the prebiological period there occurred for this synthesis the following important energetic factors: ultraviolet irradiation of the sun of about 10^{20} kilocal per year, which could reach the surface of the earth in much greater amount than at the present time, and also the energy of electrical discharges in the atmosphere. Although this latter comprises about 0.1-1.0% of the energy of the ultraviolet irradiation, yet it is an important factor in the activation of chemical reactions.

Loeb [2] in 1913 showed the formation of glycine in the silent discharge in a mixture of carbon monoxide, ammonia, and water vapor. Recently Miller [3] studied the formation of glycine, α -alanine, β -alanine, sarcosine, α -aminobutyric acid and others in the electric discharge in a mixture of methane, ammonia, hydrogen, and water vapor.

Bahadur [4] found the formation of serine, aspartic acid, valine, lysine, and other amino acids by the action of artificial illumination of a mixture of paraformaldehyde, potassium nitrate, and ferric chloride in water, and Pavlovskaya and Pasynskii [5] found formation of amino acids on ultraviolet illumination of a solution of formaldehyde, ammonium chloride, and ammonium nitrate.

In the present work we have studied the effect of cobalt and nickel ions on the formation of amino acids in a water mixture of paraformaldehyde and potassium nitrate, and also the possibility of using an organic photocatalyst, benzoyl peroxide, for this synthesis.

EXPERIMENTAL

In a 50 ml Sigcol conical flask we prepared 18 mixtures containing paraformaldehyde, potassium nitrate, and the corresponding catalyst. These flasks were divided into three groups with six flasks in each. In the first group we used cobalt chloride as the catalyst, in the second, nickel chloride, and in the third, benzoyl peroxide.

In all the flasks we weighed out 0.1 g of paraformaldehyde. In a calibrated flask we placed 0.2 g of potassium nitrate, 0.05 g of the corresponding catalyst, and brought the volume to 400 ml with distilled water. We measured out 30 ml of each solution in all six flasks of each group.

Thus, all the above mixtures contained 0.1 g of paraformaldehyde, 0.2 g of potassium nitrate, and 0.05 g of the corresponding catalyst and the total volume of each mixture was 30 ml.

All the mixtures were first studied chromatographically and it was shown that amino acids were entirely absent in them. The flasks were stoppered with surgical gauze and sterilized under a pressure of 1 atm for 30 minutes in an autoclave. After a day at room temperature the solutions were again sterilized under the same conditions.

Three flasks out of each group were covered with a thick black cloth, and the other three remained undarkened. Then all the mixtures were placed at a distance of 45 cm from a 1000 W electric lamp.

After the corresponding period of action of the electric light, as the table shows, we took one flask from each group which was submitted to the action of light and one which was not so treated, and we analyzed them for the

Catalyst	Period of illumination, hours	Conditions	Amino acid composition of mixture
CoCl ₂	119.15	In light	Valine
		In dark	Trace
	343.15	In light	Glycine
		In dark	Histidine (in sufficient amounts)
	911.0	In light	Ornithin, asparagine, arginine, aspartic acid
		In dark	Trace
NiCl ₂	119.45	In light	Trace
		In dark	Trace
	511.45	In light	Glycine, aspartic acid
		In dark	Trace
	915.00	In light	Alanine, glycine, ornithine
		In dark	Trace
Benzyl peroxide	343.00	In light	Glycine
		In dark	Trace
	511.45	In light	Glycine
		In dark	Trace
	915.00	In light	Glycine
		In dark	Trace

Note: On the chromatogram of the mixtures kept in the dark very weak rings are formed for several amino acids after prolonged reaction, but these rings are so weak that they cannot be fully interpreted.

content of amino acids by the method of circular paper chromatography [6]. Identification of the amino acids was carried out by the use of circular sheets of paper, cut radially, with simultaneous deposition of amino acid standards.

As the developer we used a mixture of butanol-acetic acid-water and as the substance for coloring we used ninhydrin in acetone.

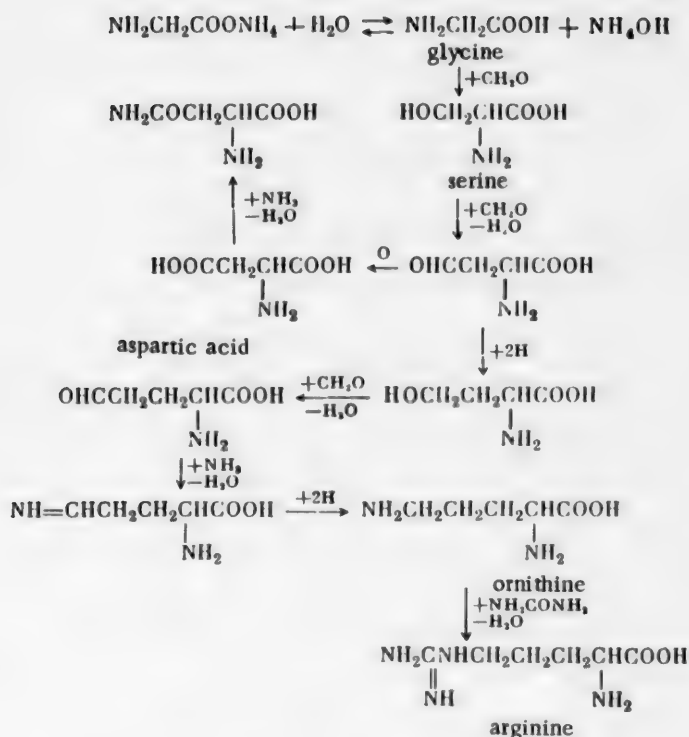
The results obtained in the analysis of the above mixtures for amino acid composition after illuminating the mixture of paraformaldehyde and potassium nitrate in the presence of various catalysts are given in the table.

DISCUSSION

These results show that illumination of a mixture which contains water, paraformaldehyde, and potassium nitrate, forms several amino acids and cobalt and nickel ions act as catalysts in this reaction. Nickel ions cause formation of a larger amount of amino acids, while cobalt ions lead to obtaining a greater number of amino acids than nickel ions, though the total amount of acids formed is less. Benzoyl peroxide also acts as a catalyst, but here only glycine is formed, and further increase in the time of illumination does not result in formation of other amino acids, although the amount of glycine increases with increasing duration of the reaction.

A study of the formation of amino acids in longer periods of illumination shows that in mixtures which contain Co⁺⁺ ions at first valine appears, and then glycine, asparagine, arginine, and aspartic acid which appears only after 911 hours of illumination. In the mixtures which contain Ni⁺⁺ ions, formation of amino acids goes slowly at first, and the first definite appearance in the mixture of glycine and aspartic acid occurs only after 511 hours of illumination. With increase in the period of illumination to 915 hours, alanine, glycine, and ornithine appear in the mixture. The quantity of amino acids in the mixture, determined by the method of circular paper chromatography, from the thickness of the band and the intensity of the color, is greatest when Ni⁺⁺ ions are used as the catalyst.

The formation of these amino acids can be explained by the following scheme, given by Bahadur [7].



Terenin [8] has found formation of free radicals in the mixture on illumination, leading to the synthesis of amino acids.

SUMMARY

On illumination of a mixture of paraformaldehyde, potassium nitrate, and distilled water in the presence of salts of cobalt or nickel with a 1000 W electric lamp, amino acid synthesis occurs. The content of amino acids increases with increased duration of the illumination.

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DICHLOROPERFLUORODIVINYL SULFIDE AND SULFIDES WITH MONOFLUOROCHLOROETHYL GROUPS

N. N. Yarovenko and A. S. Vasil'eva

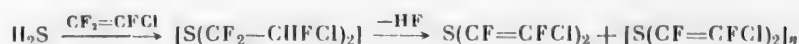
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pp. 3021-3023, September, 1961

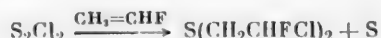
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This work was carried out in order to establish the order of addition of sulfur monochloride and hydrogen sulfide to fluorinated olefins when illuminated under pressure.

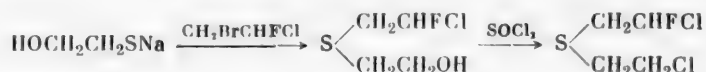
It was shown that on illumination in a glass ampule of a mixture of hydrogen sulfide and trifluorochloroethylene under pressure in the presence of benzoyl peroxide there was obtained dichloroperfluorodivinyll sulfide and its polymers.



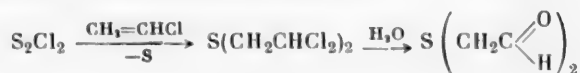
In the reaction of sulfur monochloride with vinyl fluoride under the same conditions we evidently obtain 2,2'-difluoro-2,2'-dichlorodiethyl sulfide.



The structure of these compounds was confirmed by the fact that all the C-Cl and C-F bonds were very inert. Even after many hours of stirring them in water at room temperature we did not find fluoride or chloride ions in the solution. In compounds with one 2-chloroethyl group and one 2'-fluoro-2'-chloro or 2',2'-difluoroethyl group, only one chlorine atom of the 2-chloroethyl groups was easily hydrolyzed. These compounds were obtained by reaction of 1-fluoro-1-chloro-2-bromoethane, 1-fluoro-1,2-dichloroethane, and 1,1-difluoro-2-bromoethane with sodium 2-hydroxyethylmercaptide followed by replacement of the hydroxyl group by chlorine.



The order of addition of sulfur monochloride to vinyl fluoride is indirectly confirmed by the fact that on reaction of sulfur monochloride with vinylchloride there is obtained 2,2,2',2'-tetrachlorodiethyl sulfide, hydrolyzed by water with formation of a dialdehyde, which shows its structure as



EXPERIMENTAL

2,2'-Difluoro-2,2'-dichlorodiethyl sulfide. In a 150 ml thick walled glass ampule we placed 20.3 g (0.15 mole) of sulfur monochloride and 0.2 g of benzoyl peroxide. Then the ampule was cooled with liquid air, evacuated, and connected with a reservoir of vinyl fluoride. When 18.5 g (0.4 mole) of vinyl fluoride had condensed in the ampule, it was sealed and placed at a distance of 3-5 cm from a 500 W lamp. The ampule was illuminated for 200 hours, then opened, the sulfur crystals separated, and the reaction mixture was distilled at reduced pressure. The fraction which boiled at 77-81° (9 mm) was washed several times with warm water, dried with sodium sulfate, and again distilled at 78-79° (9 mm). Yield 9 g (30%).

n_D^{25} 1.4813, d_4^{17} 1.4550.

Found %: C 24.11; H 3.41; S 16.93; F 18.74; Cl 36.0. $\text{C}_4\text{H}_6\text{SF}_2\text{Cl}_2$. Calculated %: C 24.67; H 3.08; S 16.41; F 19.49; Cl 36.41.

Colorless liquid with an unpleasant odor. Insoluble in water, easily soluble in ether, chloroform, and benzene.

2,2'-Difluoro-2,2'-dichlorodiethyl sulfo-p-toluenesulfonylimine. We shook 3.9 g (0.02 mole) of 2,2'-difluoro-2,2'-dichlorodiethyl sulfide with a solution of the chloroamine $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NNaCl} \cdot 3\text{H}_2\text{O}$ in 10 ml of water for one hour. The reaction product was filtered and washed with water. After two recrystallizations from hot alcohol we obtained 4.6 g of $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NS}(\text{CH}_2\text{CHFCl})_2$ in the form of fine white crystals with m.p. 139°.

Found %: S 17.65; F 10.65; Cl 18.98. $\text{C}_{11}\text{H}_{13}\text{O}_2\text{NS}_2\text{F}_2\text{Cl}_2$. Calculated %: S 17.60; F 10.43; Cl 19.50.

2,2,2',2'-Tetrachlorodiethyl sulfide. In a 150 ml thick walled glass ampule we placed 27 g (0.2 mole) of sulfur monochloride, 0.2 g of benzoyl peroxide, and 12.4 g (0.2 mole) of vinyl chloride. Then the ampule was sealed and placed at a distance of 3-5 cm from a 500 W lamp. After 15 days, the ampule was opened, the sulfur crystals which had separated (6.2 g) were filtered off. We obtained a dark cherry red liquid which distilled at 106° (8 mm). Yield 8.2 g (36%).

n_D^{20} 1.500, d_4^{20} 1.5823.

Found %: C 21.52; H 2.87; S 14.16; Cl 62.52. $\text{C}_2\text{H}_6\text{SCl}_4$. Calculated %: C 21.06; H 2.62; S 14.04; Cl 62.28.

The substance was yellow and had an unpleasant odor; easily soluble in ether, chloroform, and benzene; not soluble in water, but was slowly hydrolyzed.

2-Fluoro-2,2'-dichlorodiethyl sulfide. A solution of 20 g (0.2 mole) of sodium 2-hydroxyethyl mercaptide in 150 ml of alcohol was added with cooling to 32 g (0.2 mole) of 1-fluoro-1-chloro-2-bromoethane in 10 ml of alcohol. The reaction mixture stood for several hours. Then the alcohol was distilled off with small pressure reduction, and the crystals of sodium bromide were carefully washed with absolute ether. After distillation of the ether we obtained a liquid with a pale green color which was mixed with 10 g of pyridine and then with cooling was treated dropwise with 24 g of thionyl chloride and the reaction mixture was heated on an oil bath at 80-110° for several hours to remove sulfur dioxide. Then the reaction product was cooled, washed with water, and the oily liquid was dissolved in ether. The ether solution was washed successively with a weak solution of hydrochloric acid and a soda solution, dried with anhydrous sodium sulfate, and after removal of the solvent, was distilled. Yield 4.5 g (12.7%).

B.p. 102° (16 mm), n_D^{15} 1.5050, d_4^{15} 1.3301.

Found %: S 18.31; F 10.06; Cl 39.72. $\text{C}_4\text{H}_7\text{SFC}_2$. Calculated %: S 18.08; F 10.72; Cl 40.11.

2-Fluoro-2,2'-dichlorodiethylsulfo-p-toluenesulfonylimine. We shook 3.54 g (0.02 mole) of 2-fluoro-2,2'-dichlorodiethyl sulfide with a solution of 5.6 g (0.02 mole) of the chloroamine in 50 ml of water for one hour. The reaction product was filtered off and washed with water. After two recrystallizations from hot alcohol we obtained 3.2 g of sulfonylimine in the form of fine white crystals with m.p. 119.5°.

Found %: C 38.08; H 4.15; S 18.62; F 5.62; Cl 19.90. $\text{C}_{11}\text{H}_{14}\text{O}_2\text{NS}_2\text{FC}_2$. Calculated %: C 38.15; H 4.04; S 18.50; F 5.49; Cl 20.52.

2,2-Difluoro-2'-chlorodiethyl sulfide. From 26.2 g (0.262 mole) of sodium 2-hydroxyethyl mercaptide, 38 g (0.262 mole) of 1,1-difluoro-2-bromoethane, and 25 g of thionyl chloride we obtained 12 g (28.6%).

B.p. 77° (23 mm), n_D^{14} 1.4675, d_4^{14} 1.3501.

Found %: C 29.45; H 4.37; S 20.25; F 23.66; Cl 22.42. $\text{C}_4\text{H}_7\text{SF}_2\text{Cl}$. Calculated %: C 29.80; H 4.40; S 20.00; F 23.60; Cl 22.20.

Colorless liquid, not soluble in water, easily soluble in the usual organic solvents.

Tetrafluorodichlorodivinyl sulfide. In a 150 mm thick walled tube we placed 0.2 g of benzoyl peroxide, 4.5 g (0.13 mole) of hydrogen sulfide, and 26 g (0.22 mole) of trifluorochloroethylene. The ampule was sealed and placed at a distance of 10 mm from the lamp (500 W). The mixture was illuminated for about 15 days. After this the volume of the liquid phase had decreased about one third, the liquid became light yellow, and a layer of sodium fluoride appeared on the walls of the ampule. After opening the ampule the liquid was distilled and we collected the fraction with b.p. 64° (748 mm).

n_D^{20} 1.3984, d_4^{20} 1.5160.

Found %: C 20.52; S 14.14; F 33.50; Cl 31.28. $\text{C}_4\text{SF}_4\text{Cl}_2$. Calculated %: C 21.13; S 14.10; F 33.49; Cl 31.28.

The monomer of tetrafluorodichlorodivinyl sulfide easily resinified in air.

SUMMARY

1. In the case of reaction of hydrogen sulfide with trifluorochloroethylene it was shown that the fluorine-containing ethylene could react with hydrogen sulfide with formation of a halogen derivative of divinyl sulfide.
2. In the case of reaction of sulfur monochloride with vinyl chloride and fluoride it was shown that the halogenated ethylene reacts with it on illumination with evolution of elementary sulfur and formation of the corresponding halogenated dialkylsulfide.

THE SYNTHESIS AND REACTIONS OF METHYLOL AMINES OF UNSATURATED ACIDS

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We have previously studied the reaction of conversion of methylol methacrylamide under the influence of acid catalysts [1]. It was shown that when it was heated in the presence of hydrochloric acid in a dichloroethane medium, it split out water to form dimethacrylamidodimethyl ether. With increased catalyst concentration the ether was converted into methylene-bis-methacrylamide. A study of the properties of dimethacrylamidodimethyl ether showed that it has a better solubility in organic solvents than the methylene derivative and therefore is of interest as a component of copolymerization for obtaining cross connected co-polymers [2].

It is of interest to study the reaction of conversion of other methylol amide derivatives of unsaturated acids, for example, acrylic or substituted acrylic acids.

It is known that on heating methylol acrylamide in the presence of an acid catalyst, there is formation of formaldehyde and methylene-bis-acrylamide ($\text{CH}_2 = \text{CHCONH})_2\text{CH}_2$ with splitting out of water [3]. We have succeeded in directing the reaction toward splitting of water and formation of diacrylamidodimethyl ether ($\text{CH}_2 = \text{CHCONHCH}_2)_2\text{O}$.

We also synthesized the previously undescribed methylol- β, β -dimethylacrylamide by reaction of β, β -dimethylacrylic acid amide with paraformaldehyde. Methylol- β, β -dimethylacrylamide is crystalline with m.p. $81-82^\circ$, soluble in benzene and ethyl acetate and does not polymerize when heated in the presence of initiator radicals of the type of ionic catalysts. When heated in the presence of acid catalysts, it is converted into methylene-bis- β, β -dimethylacrylamide, crystals with m.p. $173.5-174.5^\circ$.

EXPERIMENTAL

Methylol acrylamide was prepared by the method of Feuer and Lynch [3]. M.p. 74° (from ethyl acetate). β, β -Dimethylacrylic acid chloride of thionyl chloride and β, β -dimethylacrylic acid [4]. β, β -Dimethylacrylamide was obtained by reaction of β, β -dimethylacrylic acid chloride with liquid ammonia [5]. M.p. $108-109^\circ$.

Diacrylamidodimethyl ether. A mixture of 10.1 g (0.1 mole) of methylacrylamide, 75 ml of carbon tetrachloride, and 0.1 ml of hydrochloric acid (d 1.19) was heated with stirring at $60-62^\circ$ for 30 minutes to precipitation of crystals. After separation from the solution and drying they gave 5.1 g (55.5%). M.p. $125.5-126^\circ$ (from ethyl acetate).

Found %: C 52.32; H 6.55; N 15.29. M 184.6. $\text{C}_8\text{H}_{12}\text{O}_3\text{N}_2$. Calculated %: C 52.14; H 6.52; N 15.27. M 184.1.

Found %: Br 63.53. $\text{C}_8\text{H}_{12}\text{O}_3\text{N}_2\text{Br}_4$. Calculated %: Br 63.25.

Methylol- β, β -dimethylacrylamide. A mixture of 10.1 g (0.1 mole) of β, β -dimethylacrylamide, 3.0 g (0.1 mole) of paraformaldehyde, 120 ml of carbon tetrachloride, and 0.032 g (0.25%) of sodium ethylate was heated with stirring at 55° for 15 minutes to obtaining an oily product. The crude product was filtered and crystallized at a temperature of about 0° . Yield 10 g (77%). M.p. $81-82^\circ$ (from ethyl acetate).

Found %: C 56.06; H 8.86; N 10.75; active H 2.08. $\text{C}_{16}\text{H}_{22}\text{O}_4\text{N}_2$. Calculated %: C 55.80; H 8.58; N 10.85; active H 2.

Found %: Br 55.20. $\text{C}_{16}\text{H}_{22}\text{O}_4\text{N}_2\text{Br}_2$. Calculated %: Br 55.32.

Methylene-bis- β,β -dimethylacrylamide. A mixture of 2.58 g (0.1 mole) of methylol- β,β -dimethylacrylamide, 60 ml of carbon tetrachloride, and 0.15 ml of hydrochloric acid (d 1.19) was heated to 60° for two hours. After removal of the solvent and drying, we obtained 1.36 g (65%). M.p. 173.5-174.5°.

Found %: C 62.24; H 8.76; N 13.32. $C_{11}H_{18}O_2N_2$. Calculated %: C 62.85; H 8.63; N 13.33.

SUMMARY

We have synthesized and characterized methylol- β,β -dimethylacrylamide. We have studied the action of acid catalysts on the methylol derivatives of acrylic and β,β -dimethylacrylic acids. We have obtained diacrylamido-dimethyl ether and methylene-bis- β,β -dimethylacrylamide.

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FLUOROMETHYL ESTERS OF SULFURIC ACID

VI. ALKYLATION OF FLUORO-SUBSTITUTED DIMETHYLSULFATES

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In a previous communication we considered processes for preparing fluorosubstituted methyl esters of sulfuric acid [1].

We showed that the alkylating ability of fluoromethyl esters of sulfuric acid depends on the number of atoms of fluorine in the sulfate molecule. Then the possibility of using the fluorine-containing dimethyl sulfate as an alkylating reagent is determined by the thermal stability.

The reaction of monofluoro- and difluorodimethyl sulfates with potassium iodide is quite difficult compared to the analogous reaction of the unsubstituted dimethylsulfate, and takes place only by heating to 50-60°. The main reaction product in both cases is methyl iodide.

Such a direction of the alkylation reaction can be explained thus, that the polarizability of the bonds of the alkyl residues with the sulfate group in the case of unsymmetrically substituted fluorine derivatives of dimethylsulfate is unequal, and on dissociation of these compounds there is a preferential ionization of the nonfluorinated methyl group, for example:



This fact is probably connected with the relative difficulty of heterolytic formation of these cations, which increases in the order $\text{CH}_3^+ > \text{CH}_2\text{F}^+ > \text{CHF}_2^+ > \text{CH}_3^+$.

It should be noted that the stability of these cations, if their formation could be determined under comparable conditions, should be changed in the contrary direction.

In discussing these results, it becomes clear that fluoromethylation and difluoromethylation can occur only when using sulfates which contain fluorine atoms in both alkoxyl groups. Actually, in the reaction of symmetrical tetrafluorodimethylsulfate with potassium iodide difluoriodomethane is formed:



However, the yield of alkylation product is not very high (25%), which is connected with the earlier discussed thermal instability of tetrafluorodimethylsulfate [2]. Just because of this fact we cannot carry out difluorination of various mineral and organic compounds.

In this connection, the high thermal stability of hexafluorodimethylsulfate leads to the possibility of using this compound as a methylating medium. However, it was shown that when hexafluorodimethylsulfate was heated with dry potassium iodide, and also with solutions of this salt in water or methanol, we did not find a trace of trifluoriodomethane and the starting sulfate was isolated in unchanged form; analogous results were obtained even when alkaline additives were used (for example, calcium carbonate) as catalysts for the alkylation reaction.

On the other hand, it was shown that hexafluorodimethylsulfate reacts with elementary iodine by four hour heating of an equimolar mixture of these reagents at 260°. Here there occurs formation of a gaseous reaction product from which we isolated trifluoriodomethane and sulfur dioxide:



Certainly this reaction has a radical character. Evidently the accumulation of fluorine atoms in the methoxyl groups of the dimethylsulfate leads to decrease (or even elimination) of the ability of the sulfate to react by electrophilic substitution. Hexafluorodimethylsulfate, like trifluoriodomethane, has the ability only for homolytic reactions. This conclusion is clearly demonstrated by the fact that when mixtures of hexafluorodimethylsulfate and iodine are heated in a quartz tube illuminated by ultraviolet light, trifluoriodomethane is formed almost quantitatively.

EXPERIMENTAL

1. Reaction of monofluorodimethylsulfate with potassium iodide. To a solution of 8 g of potassium iodide and 0.5 g of calcium carbonate in 5 ml of water at 50-60° with energetic shaking we slowly added 6.2 g of monofluorodimethylsulfate. The reaction product which separated was caught in a trap cooled to -20°. At the end of the addition of the sulfate the reaction mixture was heated to boiling. The condensate in the amount of 6.0 g (98.5%) was methyl iodide.

B.p. 42-42.5°, d_4^{20} 1.2780, n_D^{20} 1.5296.

2. Reaction of difluorodimethylsulfate with potassium iodide. In an analogous way from 4.5 g of difluorodimethylsulfate and a solution of 5 g of potassium iodide and 0.5 g of calcium carbonate in 4 ml of water at 60-65° we obtained 3.4 g (86%) of methyl iodide.

3. Reaction of tetrafluorodimethylsulfate with potassium iodide. In an analogous way from 6.6 g of tetrafluorodimethylsulfate and a solution of 8 g of potassium iodide and 0.5 g of calcium carbonate in 5 ml of water we obtained 1.5 g of difluoriodomethane with b.p. 21-22°.

Found: M 175.5. CHF_2I . Calculated: M 178.0.

4. Reaction of hexafluorodimethylsulfate with iodine. a) A mixture of 8 g of hexafluorodimethylsulfate and 8.7 g of sublimed iodine was heated in a 70 ml steel autoclave at 260° for four hours. After cooling, the autoclave was opened and the contents evaporated. The gaseous products were condensed in a trap cooled with a mixture of acetone and carbon dioxide; the uncondensed gases were collected in a gasometer. We collected in the trap about 5 ml of condensate; in the gasometer was 1.5 liters of gas; in the autoclave there remained about 6.5 g of solid residue.

The condensate was fractionated and the following fractions were isolated:

1st; b.p. -22 to -21.5°, 2.8 g of colorless gas which condensed to a colorless liquid and was trifluoriodomethane.

Found %: F 28.54. M 190.3. CF_3I . Calculated %: F 29.08. M 195.9.

2nd; b.p. -10 to -9°, 0.9 g, sulfur dioxide.

Found %: M 62.5, iodine equiv. 0.99. O_2S . Calculated %: M 64.1, iodine equiv. 1.00.

3rd; b.p. 29-30°, 3.9 g, starting hexafluorodimethylsulfate.

The residue in the autoclave was washed with cold water and was elementary iodine. In the wash water we detected sulfate ion and the absence of fluoride ion.

b) In a quartz tube we placed 8.7 g of sublimed iodine and 4 g of hexafluorodimethylsulfate. After sealing, the tube was illuminated with the light of a mercury lamp for eight hours; the reaction mixture was here heated to 80-90°. After cooling, the tube was opened and the gaseous products distilled off and passed successively through a trap cooled with ice and a wash vessel with 1 N solution of sodium hydroxide, and were condensed in a trap cooled with a mixture of acetone and carbon dioxide. The condensate in the amount of 5.8 g (89%) was redistilled and was trifluoriodomethane.

SUMMARY

We have studied the alkylating ability of some fluorine substituted dimethylsulfates and have shown that monofluorodimethylsulfate and unsymmetrical difluorodimethylsulfate have only a methylating action; symmetrical tetrafluorodimethylsulfate can be used as a difluoromethylating agent; hexafluorodimethylsulfate is capable of homolytic reaction only.

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ALKYLATION AND ARYLATION OF YELLOW PHOSPHORUS

K. A. Petrov, V. V. Smirnov, and V. I. Emel'yanov

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Attempts to use elementary phosphorus in reactions leading to the formation of organic phosphorus compounds have been made by many investigators. Carius [1] reported the preparation of tetraethyl phosphonium iodide by heating ethyl iodide with yellow or red phosphorus in a sealed tube at 150-170°. These experiments were later confirmed by other investigators [2]. It was shown that trifluoromethyl iodide can also alkylate yellow phosphorus [3]. Phosphorus was more successfully alkylated by passing the vapors of phosphorus and alkyl halide over copper powder [4].

In the present work we describe experiments on the direct alkylation and arylation of yellow phosphorus without a catalyst or activating additive, which no one had previously studied.

When benzyl chloride is heated with yellow phosphorus for four hours at 300°, benzyldichlorophosphine can be isolated from the reaction mass. Alkylation and arylation reactions evidently occur by a radical mechanism, since at high temperatures alkyl and aryl halides tend to homolytic splitting of the bond carbon-halogen.

The free radical formed attacks the molecule of yellow phosphorus, which is a tetrahedron at whose apices are arranged the phosphorus atoms, bound to each other. Phosphorus is very stable to thermal action and begins to split into two molecules of P₂ only at 800°. Thus, in the initial stages of alkylation and arylation there is rupture of P-P bonds under the action of radicals and formation of tetraphosphoradical or aryl halide, which under the influence of repeated attack by the radical particles, accompanied by rupture of the P-P bonds, change into phosphohalides.



It is interesting to explain, even though only qualitatively, the relation between the stability of the radical and the minimum temperature at which the reaction occurs. We were able to explain this effect by considering the following particles in the reaction:



whose stability with respect to effect of substituents increases on passing from left to right. It was shown that the temperature at which the reaction occurred decreased on going from the halogen derivatives which form less stable radicals to halogen derivatives which form more stable radicals: for benzyl chloride the minimum reaction temperature required was 300°, for 1-chlorophenylethane, 270°, for diphenylchloromethane, 250°, and for triphenylchloromethane, 225°.

EXPERIMENTAL

Arylation of yellow phosphorus by benzyl chloride. We heated 126.6 g (1 mole) of benzyl chloride and 15.5 g (0.5 mole) of yellow phosphorus in a sealed tube at 300° for four hours. The contents of the tube were distilled in a vacuum in a stream of dry nitrogen.

1st fraction, 52.4 g, b.p. 100-109°, n_D^{20} 1.4963, toluene.

2nd fraction, 17.5 g, b.p. 111-113° (12 mm), n_D^{20} 1.5840, d_4^{20} 1.2782, benzyldichlorophosphine (literature data, n_D^{20} 1.586, d_4^{20} 1.300 [5]). For the identification of benzyldichlorophosphine it was converted through the acid chloride of benzylphosphonic acid into benzylphosphonic acid.

Benzyldichlorophosphine was dissolved in 25 ml of dry carbon tetrachloride and dry oxides of nitrogen were passed through the solution. The solvent and excess oxides were distilled off on a water bath at atmospheric pressure, and the residue was vacuum distilled in a stream of dry nitrogen. We obtained 5.1 g of benzylphosphonic acid di-

chloride with b.p. 130° (2 mm) [6]. Then 5 g of the acid chloride was boiled for one hour in a flask with a reflux condenser with 50 ml of distilled water. When the solution was cooled, we obtained 3 g of beautiful snow white crystals of benzylphosphonic acid with m.p. 166-166.5° (from acetic acid) [7].

The third fraction, 1.1 g, b.p. 234-236° (12 mm) was dibenzylchlorophosphine [6]. For identification, 1 g of the substance was boiled for one hour with 6 ml of 6% hydrogen peroxide in a flask with a reflux condenser. On cooling, the solution precipitated 0.77 g of dibenzylphosphinic acid in the form of mother-of-pearl colored plates with m.p. 191-192° (from alcohol) [7].

The residue, a dark tar, was boiled for 1-5 hours with an alkaline solution of hydrogen peroxide (40 ml of 6% H_2O_2 and 110 ml of 2 N HCl) in a flask with a reflux condenser. The alkaline solution was filtered from the tarry residue, neutralized with dilute hydrochloric acid (1 : 1) and excess acid was added. The resulting yellow precipitate was twice crystallized from hot alcohol. We obtained 0.75 g of dibenzylphosphinic acid with m.p. 191-192° [7].

From the tarry residue insoluble in alkaline hydrogen peroxide we separated a small amount of stilbene by steam distillation.

Arylation of yellow phosphorus with bromobenzene. We heated 157 g (1 mole) of bromobenzene and 15.5 g (0.5 mole) of yellow phosphorus in a sealed tube for four hours at 350°. The contents of the tube were distilled in a vacuum in a stream of dry nitrogen. At first a small amount of colorless liquid with b.p. 42-43° (10 mm) came over; then we collected two fractions.

The first fraction, 58.65 g, was a yellow liquid with b.p. 126-128° (11 mm), n_D^{20} 1.6533, d_4^{20} 1.8732, phenyldibromophosphine (literature data: b.p. 132° at 14 mm [8]). For identification we passed dry oxides of nitrogen into a solution of 57 g of the substance in 25 ml of carbon tetrachloride. The excess oxides of nitrogen and solvent were distilled off on a water bath. The residue was distilled in a vacuum. We obtained 41.6 g of a yellow, oily liquid with b.p. 156-158° (12 mm), n_D^{20} 1.6177, d_4^{20} 1.9452, which was phenylphosphonic acid dibromide [8].

We heated 36 g of the dibromide for one hour with 50 ml of water in a flask with a reflux condenser. When the solution was cooled, 18 g of phenylphosphonic acid with m.p. 160° (from aqueous alcohol) [8] precipitated.

The second fraction, 30 g, was a yellow liquid with b.p. 179-180° (12 mm), n_D^{20} 1.6713, d_4^{20} 1.4707, diphenyldibromophosphine [9]. For identification the substance was dissolved in 15 ml of carbon tetrachloride and dry oxides of nitrogen were passed in. The oxidation product did not distil at 270° (10 mm). We heated 18.3 g of the reaction mixture for one hour in a flask with a reflux condenser with 50 ml of 40% methanol; the hot solution was filtered. On cooling, it precipitated 10.5 g of diphenylphosphinic acid with m.p. 191-192° [8].

The residue, a dark oil, was extracted with ether. After evaporation of the solvent, the extract gave a thick red oil which did not crystallize on standing. The portion insoluble in ether (9.5 g) was boiled for one hour in a flask with a reflux condenser with an alkaline solution of hydrogen peroxide. The residue darkened and almost completely dissolved. The solution was extracted with ether. We obtained from the ether extract 0.1 g of needles of triphenylphosphine oxide with m.p. 152-153° (from ligroin) (literature data: m.p. 153° [10]).

From the precipitate obtained by acidification of the alkaline solution, after recrystallization from aqueous methanol, we isolated some crystals with melting point close to that of diphenylphosphinic acid.

Arylation of yellow phosphorus by m-bromotoluene. We heated 50 g (0.3 mole) of m-bromotoluene and 3.1 g (0.1 mole) of yellow phosphorus in a sealed tube at 300° for four hours. At the end of the heating there was a precipitate of red phosphorus in the tube. The reaction mixture was distilled in a vacuum in a stream of dry nitrogen. At first a considerable amount of starting bromotoluene distilled over, and then we collected two fractions.

The first, 16.4 g, was m-tolyldibromophosphine, with b.p. 110-111° (2 mm); the second, 6.1 g, was di-m-tolyldibromophosphine with b.p. 141-142° (2 mm).

Alkylation of yellow phosphorus with n-octyl bromide. We heated 40 g (0.2 mole) of octyl bromide and 2.14 g (0.07 mole) of yellow phosphorus in a sealed tube at 250-270° for 3.5 hours. The reaction mixture was distilled in a vacuum in a stream of dry nitrogen. We distilled off 19.5 g of octylene (b.p. 125-127°). We collected two fractions: the first, 6 g, was n-octyldibromophosphine with b.p. 72° (22 mm); the second, 3.1 g, was di-n-octyldibromophosphine with b.p. 140° (11 mm).

SUMMARY

1. We have suggested a method for synthesis of halogen derivatives of alkyl and aryl phosphines.
2. We have described for the first time the direct arylation of yellow phosphorus by aryl halides.

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STUDIES IN THE NAPHTHALENE SERIES

XXII. AMINATION OF DIHYDROXYNAPHTHALENES*

V. K. Kozlov and I. K. Veselovskaya

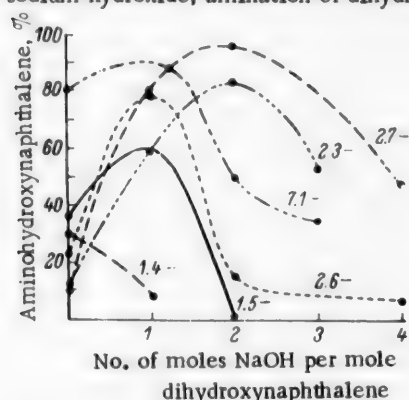
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The reaction of amination of α - and β -naphthols [1], their naphtholates and ethers can be extended to the isomeric dihydroxynaphthalenes.

The experiments on amination of the dihydroxynaphthalenes were carried out in an autoclave with 25% ammonia for 1-6 hours at 180-250°. The reaction took place with formation of naphthalene diamines and aminonaphthols. At a comparatively low temperature (180°) the most easily aminated dihydroxynaphthalenes were those with hydroxy groups in one ring of the naphthalene (1,2-, 1,4-, 2,3-). Conversion of 1,4- and 1,8-dihydroxynaphthalenes was complicated by formation of products of condensation of the starting substance and by tars. The amination reaction was carried out in the presence of 1-4 moles of sodium hydroxide with formation of incomplete and complete naphtholates and led to a sharp decrease in yield of naphthylene diamines. In experiments with 1,5- and 1,7-dihydroxynaphthalenes, naphthylene diamines were not formed even with 1 mole of sodium hydroxide, and in experiments with 2,6- and 2,7 isomers, at 2 moles of sodium hydroxide. It was most interesting that in the presence of sodium hydroxide, amination of dihydroxynaphthalenes could be stopped at the aminonaphthalenes, which were formed



Effect of NaOH on yield of aminohydroxynaphthalenes in amination by 25% NH_4OH (3 hours at 250°).

in considerable yield [3]. Thus, the yield of aminonaphthols reached its maximum value for the isomers 1,7-; 2,6-; and 1,5 (respectively 90, 79, and 60%) at mole ratio of sodium hydroxide to dihydroxynaphthalene of 1 : 1, and for 2,7-dihydroxynaphthalene, at a ratio of 2 : 1 (93.2%). On further increase in the amount of sodium hydroxide, the yield of aminonaphthols fell sharply. This was especially the case for α,α -dihydroxynaphthalene, and to a less degree for the α,β - and still less for the β,β -isomers (figure).

In the amination of 1,7-dihydroxynaphthalene we obtained 7-amino-1-naphthol (monoacetyl derivative m. 211°) [4]. On amination in the presence of sodium hydroxide, decrease in the reaction temperature for 1,7-dihydroxynaphthalene from 250 to 180° led to a sharp decrease in the amount of aminonaphthol (from 79.5% to 29.2%). For 2,7-dihydroxynaphthol the amount of aminonaphthol fell from 80% to 16.5%.

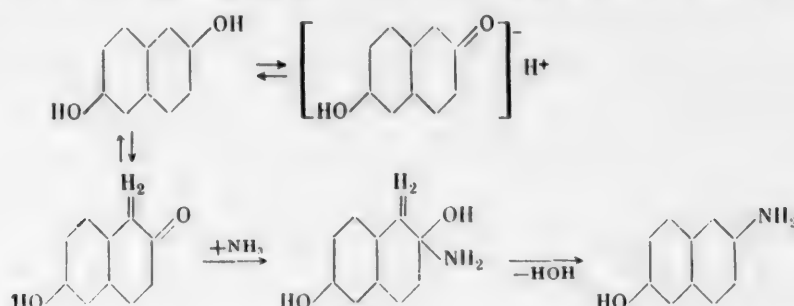
On amination in the presence of sodium hydroxide the yield of product also depends on the time of heating. Thus, on decreasing the time of amination of 2,7-dihydroxynaphthalene (NaOH 2 : 1, 250°) from three to one hour, the yield of aminonaphthol fell from 93.2 to 58.7%. Increase in the time of amination of 1,5-dihydroxynaphthalene (NaOH 1 : 1, 250°) from three to six hours led to an increase in yield of aminonaphthol from 60 to 70.9%.

Thus, the behavior of the dihydroxynaphthalenes in the reaction of amination with sodium hydroxide is entirely analogous to that observed for the naphthols and their naphtholates [2].

The preferential formation of the aminonaphthols in the amination of the dihydroxynaphthalenes in the presence of sodium hydroxide is connected with the decreased activity of dihydroxy compounds in the "fixed" enol form

* Communication XXI, see ZhOKh, 31, 2485 (1961).

of the naphtholates. It is quite possible that the different degrees of amination for different isomeric dihydroxy-naphthalenes depend on the different stability of the naphtholate groups to hydrolysis and the different dissociations in an alkaline medium with the formation of negative ions [5]. Only the undissociated enol form and its shift to the formation of the keto form permits the replacement of both or one hydroxy group by an amino group.



The significance of the enol function of the hydroxyl for explaining the unusual transformations which occur with the multinuclear disubstituted naphthalenes was studied by N. N. Vorozhtsov [6]. The observed stepwise reaction in obtaining products from such dihydroxy- or diamino substituted compounds as a result of the sulfite reaction or amination in an alkaline medium was a consequence of the fact that in multiring disubstituted compounds only one ring reacted in the keto form. Such sorts of stable monobisulfite compounds which corresponded to the mono-keto form were obtained for 1,5- and 2,7- [7] and 1,4- and 1,2-dihydroxynaphthalenes [8]. Comparison of the fullness of amination of the isomeric dihydroxynaphthalenes both with ammonia alone and in the presence of sodium hydroxide shows that the greatest ability for such a reaction is possessed by dihydroxynaphthalenes with a quinogenic arrangement of the substituents. At high temperatures the greatest amination activity is found for 2,6- and 2,7-isomers. β,β -Dihydroxynaphthalenes are aminated more easily than the α,α -isomers. On amination of the α,β -dihydroxynaphthalenes there first occurs formation of α -hydroxy- β -naphthylamines (for the 1,7-isomer, 7-amino-1-hydroxy-, and for the 1,2-isomer, 2-amino-1-hydroxy-).

EXPERIMENTAL

Amination of the dihydroxynaphthalenes. The experiments on heating 8 g (0.05 mole) of dihydroxynaphthalene isomers with 50 ml of 25% ammonia were carried out in a horizontal rotating steel autoclave (capacity 150 ml) without a stirrer. The temperature was increased to the desired level after 30 minutes and was then maintained. After heating, the contents of the autoclave were extracted with 75-100 ml of water, the precipitate was filtered off and washed with 5% sodium hydroxide solution. For most of the dihydroxynaphthalenes this precipitate consisted of the corresponding naphthylene diamine. Only for 1,8-dihydroxynaphthalene in this case was there a black, powdery precipitate which had no melting point, dissolved neither in sodium hydroxide nor hydrochloric acid, and did not contain nitrogen. This product was assumed to be a condensation product of the dihydroxynaphthalene. 1,8-Naphthylene diamine occurred partly in the form of a mobile oil, partly in solution from which it was separated by neutralization of the alkaline solution, also as an oil. For separation from admixed dihydroxynaphthalene, this oil was extracted with ether. On saturation of the ether solution with hydrogen chloride 1,8-naphthylene diamine hydrochloride with m.p. about 240° separated.

After separation of the diamidonaphthalenes, the mother alkaline liquors and the alkaline wash water were combined and neutralized with hydrochloric acid to an acid reaction to Congo paper. The dihydroxynaphthalene which precipitated was filtered off, washed with a small amount of cold water, and dried in a desiccator. The acid filtrate and wash water were combined and treated with 10% sodium carbonate or sodium acetate to a weak acid reaction to litmus. The aminonaphthols which then precipitated were filtered off and dried in a desiccator.

The dihydroxynaphthalenes were obtained as described in the literature, with melting points corresponding to the pure substances (1,5- -261°; 1,7- -178°; 2,6- -218°; 2,7- -187°; 1,8- -141°; 2,3- -161°). The isomeric naphthylene diamines and aminonaphthols isolated in the amination process were recrystallized to constant melting point, which agreed with the literature values. For some of the aminonaphthols we prepared the monoacetyl derivatives which had sharper melting points.

Aminonaphthols: 1,5- -193°; 1,7- -130°; 2,6- -201°; 2,7- -195°; 1,8- -96°; 2,3- -234°.

Amination of Dihydroxynaphthalenes 8 g (0.05 mole); 50 ml (0.8 mole) 25% NH_4OH ; 3 hours

No.	Dihydroxy-naphthalene isomer	Reaction temperature	Moles NaOH used	Isolated, %		
				Diamine	Amino-naphthol	Dihydroxy-naphthalene
1	1,2-	180°	—	44.3	39.6	—
2	1,2-	180	0.05	—	100.0	—
3	1,4-	180	—	15.9	29.4	52.0
4	1,4-	180	0.05	—	8.5	37.2
5	1,5-	250	—	25.9	36.1	29.6
6	1,5-	250	0.05	—	60.0	39.4
7	1,7-*	250	0.05	—	70.9	24.0
8	1,7-	250	—	21.5	79.5	—
9	1,7-	250	0.05	—	90.0	—
10	1,7-	180	0.05	—	29.5	71.2
11	1,8-	210	—	58.5	17.9 **	12.5
12	1,8-	250	—	43.2	23.1 **	13.7
13	1,8-	210	0.05	—	12.2 **	77.5
14	1,8-	180	—	—	16.2 **	75.9
15	2,3-	180	—	49.0	35.6	2.2
16	2,3-	250	—	72.2	12.6	—
17	2,3-	250	0.05	19.6	58.8	20.0
18	2,3-	150	0.10	—	83.0	17.0
19	2,3-	150	0.15	—	53.1	36.7
20	2,6-	150	—	62.5	23.1	—
21	2,6-	150	0.05	—	78.8	12.0
22	2,7-	150	—	80.0	4.6	—
23	2,7-	150	0.05	—	80.0	20.0
24	2,7-	150	0.1	—	93.2	—
25	2,7-	200	0.05	—	16.5	77.7

* Experiment carried out in the course of six hours.

** Yield shown is not aminonaphthol, but the condensation product of the dihydroxy-naphthalene.

Naphthylene diamines: 1,2- -94°; 1,4- -120°; 1,5- -189°; 1,7- -116°; 2,3- -192°; 2,6- -217°; 2,7- -162°.

In the table we give average results from two parallel experiments.

SUMMARY

1. We have carried out comparative aminations of isomeric dihydroxynaphthalenes with formation of a mixture of naphthylene diamines and aminonaphthols. Amination in the presence of sodium hydroxide permits limiting the reaction chiefly to the formation of aminonaphthols.

2. The greatest ability for amination occurs in the dihydroxynaphthalenes with a quinogenic arrangement of the hydroxy groups. At higher temperatures the greatest amination activity is found for the 2,6- and 2,7-isomers.

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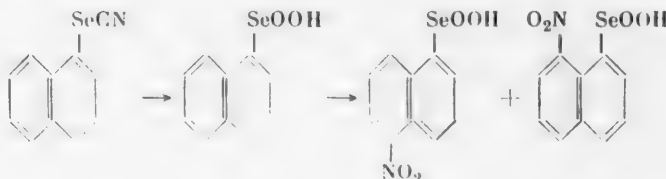
STUDIES IN THE NAPHTHALENE SERIES.

XXIII. THE OXIDATIVE NITRATION OF α -SELENOCYANONAPHTHALENE
AND α,α' -NAPHTHALENE DISELENIDE*

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It has been known that when β -selenocyanonaphthalene, $C_{10}H_7SeCN$, was heated with 20% nitric acid it was smoothly oxidized to β -naphthylseleninic acid $C_{10}H_7SeOOH$ [1]. Under analogous conditions in the case of α -selenocyanonaphthalene [2] instead of the expected and undescribed α -seleninic acid we obtained its nitro derivative. We have shown [3] that with 15 hour heating on a boiling water bath of α -selenocyanonaphthalene and 20% nitric acid the chief reaction products are 1,5- and 1,8-nitroseleninic acids with yields up to 52-60% at a ratio of isomers 2 : 3. The total yield of both substances was established by their isolation in the form of the lead salts. The isolation of the separate isomers [4] was carried out by fractional crystallization of the free nitroseleninic acids, of which the 1,5-isomer is better soluble than the 1,8-isomer. Formation of these compounds can occur according to the scheme:

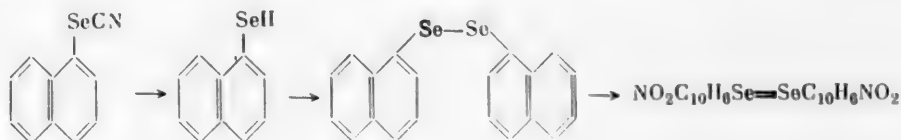


Although under severe reaction conditions α -seleninic acid was not found, the oxidation of the $SeCN$ group should precede the nitration reaction by 20% nitric acid. The ratio of pure 1,5- and 1,8-nitroselenocyanonaphthalenes to 20% nitric acid confirms this [4].

Experiments on the action of 60% nitric acid on α -selenocyanonaphthalene at 20-40° for three hours led to formation of its mononitro substituents.

Beside the isomeric naphthyl nitroseleninic acids we isolated from the reaction medium the following products of oxidation and nitration of α -selenocyanonaphthalene: 5,5'- and 8,8'-dinitro-1,1'-dinaphthyldiselenide; 1,1'-dinaphthyldiselenide, some unchanged starting substance, and some tar. The total amount of all the products of oxidation and nitration of selenocyanonaphthalene was 94-96%.

The formation of the side products can be explained by supposing that there first occurs transformation of the $SeCN$ group into SeH with formation of α -selenonaphthol. This is a very unstable substance [5], which can quickly be oxidized to 1,1'-dinaphthyldiselenide, which is further nitrated with formation of a mixture of isomeric dinitro-1,1'-dinaphthyldiselenides.



* Communication XXII, see ZhOKh, 31, 2826 (1961).

TABLE. Products of the Oxidative Nitration Reaction of α -Selenocyanonaphthalene

Nitroselenenic acid, %		Unchanged α -seleno- cyanonaph- thalene, %	1,1'-Dinaph- thyldiselenide, %	Mixture of isomeric dinitro- 1,1'-dinaphthyl- diselenides, %
1,5-	1,8-			
22.1	31.4	14.6	6.7	11.6

It is not very likely that under the reaction conditions there would be partial oxidation of the dinitrodinaphthyl-diselenides to the corresponding nitroselenenic acids of naphthalene, since it is known that diselenides are comparatively stable compounds [1]. According to our experiments, formation of naphthalene nitroselenenic acids from α, α' -dinaphthyl-diselenides was possible only by heating with fuming nitric acid. Here the yield of 1,5- and 1,8-naphthalene nitroselenenic acids reached 84% with a ratio of isomers 2 : 3. Thus, naphthalene nitroselenenic acids are formed according to the first scheme. The sum of the products of the oxidative nitration reaction of α -selenocyanonaphthalene is shown in the table (average of three experiments).

The results of the oxidative nitration of α -selenocyanonaphthalene show that the orienting effect of the SeOOH is analogous to the orienting effect [6] of the SOOH or SO₂OH groups.

EXPERIMENTAL*

Preparation of α -selenocyanonaphthalene. Five g of α -naphthylamine (m.p. 49°) was dissolved in 15 ml of hot water, then 10 ml of concentrated hydrochloric acid was added and the mixture was heated to 50° for full solution of the amine. The resulting solution was poured onto 60 g of ice and diazotized at 0-5° with a solution of 2.5 g of sodium nitrite and 20 ml of water. The diazo solution was treated with sodium acetate to weak acid reaction to Congo. The filtered solution was added slowly with stirring to a solution of 10 g of KSeCN in 100 ml of water. After it had stood for three hours, the tarry precipitate was filtered off, washed, and dissolved in 60 ml of 80% acetic acid and again separated by pouring into 200 ml of water. Repeated crystallizations from 90% acetic acid gave the substance in the form of prismatic needles of a light brown color, m.p. 72°.

Found %: C 37.01; H 3.08; N 6.15; Se 33.92. $C_{11}H_7NSe$. Calculated %: C 56.9; H 3.00; N 6.03; Se 34.05.

Oxidation of α -selenocyanonaphthalene. Five g of α -selenocyanonaphthalene and 50 ml of 20% nitric acid were heated for 15 hours in a flask with a reflux condenser on a boiling water bath. At the end of the heating, the liquid had separated into layers. The upper layer, clear and light yellow, was mixed with a tarry, dark red mass. On evaporation of the clear solution and fractional crystallization of the resulting precipitate, we obtained a substance in the form of light yellow needles with m.p. 196-198° which gave no melting point depression when mixed with 1-nitro-8-naphthaleneselenenic acid. From the mother liquor after strong evaporation we isolated a substance in the form of fine needles with m.p. 140-145° which gave no melting point depression when mixed with 1-nitro-5-naphthaleneselenenic acid. Separation of the isomers was difficult, and we often isolated a mixture of them with m.p. 160-165°, in which the 1,8-isomer predominated, and a mixture with m.p. 121-125° in which the 1,5-isomer predominated.

We dissolved 3.1 g of the tarry mass with heat in 150 ml of water and filtered the insoluble precipitate. When the solution was cooled to 60-70°, 0.05 g of a product precipitated, having a yellow-orange color and m.p. 86°, corresponding in properties to α, α' -dinaphthyl-diselenide [4]. When the water solution was cooled completely, and also on evaporation of the water mother liquor a precipitate came down from which after fractional crystallization we were able to obtain a further quantity of the 1,5- and 1,8-naphthalene nitroselenenic acids. In all from the reaction mass we isolated 1.24 g of the 1,5-isomer and 1.76 g of the 1,8-isomer. The water insoluble residue from the treatment of the tarry mass, 2.3 g, was dissolved in hot alcohol and filtered from the residue. When the alcohol solution cooled, 0.65 g of a product with m.p. 41-45° came down. After repeated crystallization from alcohol the product melted at 49-51°, contained nitrogen, and most probably was a mixture of isomeric dinitrodinaphthyl-diselenides.

Found %: Se 30.4. $C_{20}H_{12}O_4N_2Se_2$. Calculated %: Se 31.5.

* With participation of G. D. Vlahov.

By dilution of the first alcoholic mother liquor with water we precipitated 0.33 g of a product with a yellow-orange color and m.p. 85°, corresponding to α,α' -dinaphthyldiselenide. The product insoluble in alcohol (see above), 1.2 g, was recrystallized from 50% acetic acid. We obtained 0.9 g of substance in the form of light brown needles with m.p. 71°, corresponding to α -selenocyanonaphthalene.

Quantitative separation of the mixture of isomeric naphthalene nitroseleninic acids was carried out using their lead salts. Oxidation by 20% nitric acid of 12 g of α -selenocyanonaphthalene, carried out as above, gave 4.5 g of a tarry mass and 47 ml of light colored nitric acid solution. The latter was neutralized with soda, made weakly acid with hydrochloric acid, and treated with a 1 N solution of lead nitrate. We separated 12.05 g of lead salts (salt of the 1,8-acid, needles, salt of the 1,5-acid, plates). By analogous treatment of the tarry mass we separated from it 0.95 g of mixed lead salts of the isomeric naphthalene nitroseleninic acids. In all we separated 13 g (63.5%) of the lead salts.

Oxidative nitration of α,α' -dinaphthyldiselenide. Seven g of α,α' -dinaphthyldiselenide, m.p. 83°, was obtained from α -bromonaphthalene by the Grignard synthesis [4], placed in a round bottomed flask with a long neck, and treated with 12 ml of nitric acid (d 1.52). After heating for one hour over a weak flame, the mass was carefully diluted with 100 ml of water. The yellow product which precipitated (6 g) was filtered off, washed with cold water, then with alcohol, and dried. By alternate recrystallization from acetic acid and alcohol we obtained two substances: the first with m.p. 145° (needles) the other 198° (plates), which showed no melting point depression mixed with the 1,5- and 1,8-naphthalene nitroseleninic acids respectively.

SUMMARY

We have studied the oxidative nitration by 20% nitric acid of α -selenocyanonaphthalene leading to the formation as the chief reaction products of 1,5- and 1,8-naphthalene nitroseleninic acids. The same substances are obtained by oxidative nitration with fuming nitric acid of α,α' -dinaphthyldiselenide.

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THE SYNTHESIS OF UNSATURATED KETONES WHICH CONTAIN THE FURAN RING

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Many of the unsaturated ketones which are derivatives of furan and their 2,4-dinitrophenylhydrazones have not been described up to now. Also there are contradictory data on physical properties for some which have been prepared, especially as to their melting points, and, as our study has shown, many of them were not carefully purified.

The synthesis of unsaturated ketones which contain benzene and furan rings is most easily carried out by crotonic condensation of the corresponding methyl ketones with aldehydes by the scheme [1-8]:



where R and R₁ are radicals of the aromatic and furan series.

It is interesting to see that in this reaction, for the purpose of obtaining furan derivatives, up to now have been used chiefly furfural and furylacrolein, while 2-acetylfuran has been condensed only with benzaldehyde [9] and some other aldehydes. We have widened the field by the use of 2-acetylfuran for the synthesis of unsaturated ketones, by reacting it with furylacrolein, 2,4-dimethoxybenzaldehyde, cinnamic, 4-methoxycinnamic, and 2,4-dimethoxycinnamic aldehydes.

We have also obtained all the possible isomers of 1-furyl-3-phenylpropenone, 1-furyl-5-phenylpentadienone, and their 5-methoxy and 2,4-dimethoxy derivatives with different positions of the carbonyl group and conjugated system of double bonds, and also 1,3-difurylpropenone and two 1,5-difurylpentadienones.

All these ketones were carefully purified and characterized as the 2,4-dinitrophenylhydrazones; the latter were obtained by the usual method [12].

The unsaturated ketones containing the furan ring which we have synthesized are colorless or yellowish solid crystalline substances; with mineral acids they form intensely colored solutions from orange-red to red-violet in color. All are easily soluble in alcohol, ether, and other organic solvents and are insoluble in water. The main information on these products is given in the table.

EXPERIMENTAL

Crotonic condensation. Stoichiometric amounts of the corresponding methyl ketone (0.01 mole) and aldehyde were dissolved in a small amount of alcohol (10-20 ml), and 2-5 ml of a 5-10% sodium hydroxide solution was added gradually dropwise with stirring. The mixture of reacting substances stood for 18-24 hours at room temperature. The resulting precipitate was filtered off, washed with aqueous alcohol (50-80%), and recrystallized with the use of activated charcoal to constant melting point. The product was dried in the dark and in a vacuum.

2,4-Dinitrophenylhydrazones were obtained by mixing equimolecular amounts of alcoholic solutions of the unsaturated ketone with hydrochloric acid solutions of 2,4-dinitrophenylhydrazine with short heating on a water bath. The precipitate was filtered off, washed with hydrochloric acid, alcohol, ether, and was recrystallized from a mixture of benzene and methyl alcohol to constant melting point.

SUMMARY

By the method of crotonic condensation we have prepared in good yields from 2-acetylfuran, 2-furylacrolein, furfural, and aromatic aldehydes the corresponding propenones and pentadienones of the furan series. We have synthesized a number of compounds not described in the literature and in some cases have corrected the melting point.

Ketone	Starting substance	M.p.*	Yield, %	Appearance and crystal form of ketone	2,4-Dinitrophenylhydrazones									
					Empirical formula	% C		% H		m. p.	color	empirical formula	% N	
						calc.	found	calc.	found				calc.	found
1-Furyl-3-phenyl-1-propenone	2-Acetylfuran and benzaldehyde	89° [10, 11, 9, 13]	86	Colorless plate-like crystals	C ₁₅ H ₁₀ O ₂	—	—	—	—	214-215°	Bright red	C ₁₅ H ₁₀ O ₂ N ₄	14.80	14.89
1-Furyl-3-phenyl-3-propenone	Furfural and acetophenone	37.5°	90	Fine yellow crystals	C ₁₅ H ₁₀ O ₂	—	—	—	—	221	Red	C ₁₅ H ₁₀ O ₂ N ₄	14.80	14.82
1,3-Difurylpropenone	Furfural and acetylfuran	89-90° [10, 19]	92	Colorless plate-like crystals	C ₁₁ H ₈ O ₃	—	—	—	—	205-206	Brown	C ₁₇ H ₁₂ O ₆ N ₄	15.20	15.25
1-Furyl-3-(4'-methoxyphenyl)-1-propenone	2-Acetylfuran and anisaldehyde	83 [11]	92	Light yellow needle-like crystals	C ₁₆ H ₁₂ O ₃	—	—	—	—	196-198	Red	C ₂₀ H ₁₆ O ₆ N ₄	13.71	13.70
1-Furyl-3-(4'-methoxyphenyl)-3-propenone	Furfural and 4-methoxyacetophenone	81.5°	84	Light yellow rhombic crystals	C ₁₆ H ₁₂ O ₃	—	—	—	—	183-184	Bright red	C ₂₀ H ₁₆ O ₆ N ₄	13.71	13.72
1-Furyl-3-(2',4'-dimethoxyphenyl)-1-propenone	2-Acetylfuran and 2,4-dimethoxybenzaldehyde	86.5	30	Fine light crystals	C ₁₅ H ₁₀ O ₄	69.76	69.57	5.46	5.44	226-227	Bright red	C ₂₁ H ₁₆ O ₇ N ₄	12.77	12.81
1-Furyl-3-(2',4'-dimethoxyphenyl)-3-propenone	Furfural and 2,4-dimethoxyacetophenone	59.5-60	86	Light yellow needle-like crystals	C ₁₅ H ₁₀ O ₄	69.76	69.86	5.46	5.32	205.5	Bright red	C ₂₁ H ₁₆ O ₇ N ₄	12.77	12.82
1-Furyl-5-phenyl-2,4-pentadien-1-one	2-Acetylfuran and cinnamaldehyde	112-113	96	Light scales	C ₁₅ H ₁₂ O ₂	80.34	80.17	5.39	5.43	198-199	Dark red	C ₂₁ H ₁₆ O ₅ N ₄	13.86	13.86
1-Furyl-5-phenyl-1,3-pentadien-3-one	Furfural and benzalacetone	56-57 [1, 4, 14] (from ligroin)	87	Light yellow plates	C ₁₅ H ₁₂ O ₂	—	—	—	—	175	Crimson	C ₂₁ H ₁₆ O ₅ N ₄	13.86	13.88
1-Furyl-5-phenyl-1,3-pentadien-5-one	Furylacrolein and acetophenone	61°	85	Yellow plate-like crystals	C ₁₅ H ₁₂ O ₂	—	—	—	—	217 (decomp)	Red	C ₂₁ H ₁₆ O ₅ N ₄	13.86	13.89
1,5-Difuryl-2,4-pentadien-1-one	2-Acetylfuran and furfural	82	80	Light yellow needle-like crystals	C ₁₅ H ₁₀ O ₃	72.88	72.50	4.72	4.63	187	Brown	C ₁₉ H ₁₄ O ₆ N ₄	14.20	14.18
1,5-Difuryl-1,3-pentadien-3-one	Furfural and acetone	61-62 [4, 22, 23, 24] (from petroleum ether)	80	Yellow needle-like crystals	C ₁₅ H ₁₀ O ₃	—	—	—	—	195	Dark brown	C ₁₉ H ₁₄ O ₆ N ₄	14.20	14.37
1-Furyl-5-(4'-methoxyphenyl)-2,4-pentadien-1-one	2-Acetylfuran and 4-methoxycinnamaldehyde	144.5	80	Light yellow needle-like crystals	C ₁₆ H ₁₂ O ₃	75.58	75.08	5.54	5.55	215	Brown	C ₂₂ H ₁₈ O ₆ N ₄	12.89	12.91
1-Furyl-5-(4'-methoxyphenyl)-1,3-pentadien-3-one	Furfural and anisalacetone	84 [24] (from ligroin)	89	Bright yellow needle-like crystals	C ₁₆ H ₁₂ O ₃	—	—	—	—	174-175	Dark red	C ₂₂ H ₁₈ O ₆ N ₄	12.89	12.82
1-Furyl-5-(4'-methoxyphenyl)-1,3-pentadien-3-one	Furylacrolein and 4-methoxyacetophenone	98.5	88	Yellow needle-like crystals	C ₁₆ H ₁₂ O ₃	75.58	76.02	5.54	5.84	189.5-190.5	Brown	C ₂₂ H ₁₈ O ₆ N ₄	12.89	12.82
1-Furyl-5-(2',4'-dimethoxyphenyl)-2,4-pentadien-1-one	2-Acetylfuran and 2,4-dimethoxycinnamaldehyde	116	78	Light orange prismatic crystals	C ₁₇ H ₁₄ O ₄	71.83	71.56	5.66	5.54	208-209	Dark brown	C ₂₃ H ₂₀ O ₇ N ₄	12.07	12.13
1-Furyl-5-(2',4'-dimethoxyphenyl)-1,3-pentadien-3-one	Furfural and acetone and 2,4-dimethoxybenzaldehyde	100.5	92	Light yellow needle-like crystals	C ₁₇ H ₁₄ O ₄	71.83	72.26	5.66	5.83	189-190	Violet	C ₂₃ H ₂₀ O ₇ N ₄	12.07	12.14
1-Furyl-5-(2',4'-dimethoxyphenyl)-1,3-pentadien-5-one	Furylacrolein and 2,4-dimethoxyacetophenone	131-132	93	Light yellow prismatic crystals	C ₁₇ H ₁₄ O ₄	71.83	72.08	5.66	5.52	204.5	Bright red	C ₂₃ H ₂₀ O ₇ N ₄	12.07	12.10

* Crystallized from aqueous alcohol.

** Crystallized from petroleum ether; according to the literature, m.p. 26° [15], 35° [16], 46° [10, 17], 47° [18].

*** According to the literature, m.p. 75° [20], 79-81° [21], 79° [2, 22].

**** According to the literature, m.p. 52-53° [5].

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THE MECHANISM OF THE FORMATION OF 2-PHENYL- 2-HYDROXY-1,3-INDANDIONE FROM DIBROMOBENZALPHTHALIDE

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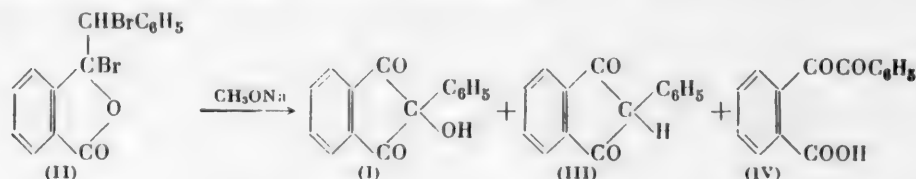
Translated from *Zhurnal Obshchei Khimii*, Vol. 31, No. 9,

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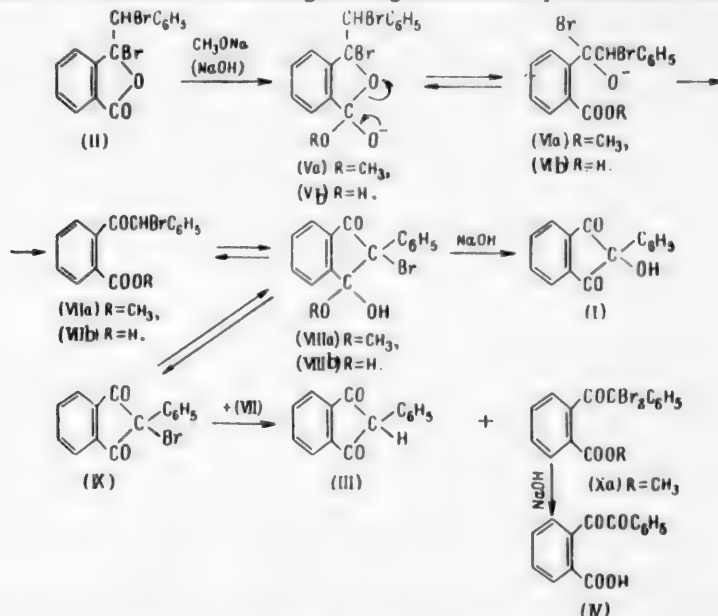
2-Hydroxy-2-phenyl-1,3-indandione (I) was first obtained by Gabriel [1] by the action of sodium methylate on dibromobenzalphthalide (II). According to his proposed method, the initial dibromobenzalphthalide is dissolved in a 2% sodium methylate solution; after 30 minutes, water is added to the reaction mixture and a current of carbon dioxide is passed through it for several hours. The precipitate of 2-hydroxy-2-phenyl-1,3-indandione (I) is filtered and then rapidly recrystallized in a current of inert gas.

When 2-hydroxy-2-phenyl-1,3-indandione was obtained by this method it was found that the process is very complex and the yield less than 20%, because the main reaction products are 2-phenyl-1,3-indandione (III) and o-carboxybenzil (IV) (the yields being 31 and 33% respectively). Furthermore, for reasons unknown, 2-hydroxy-2-phenyl-1,3-indandione is often not obtained at all in this reaction.



These facts prompted us to investigate the mechanism of this reaction and also to attempt to find more reliable methods of obtaining 2-hydroxy-2-phenyl-1,3-indandione (I).*

These investigations made it possible to propose the following system of the process of formation of 2-hydroxy-2-phenyl-1,3-indandione (I), a number of these stages being established by the author's experiments.



* It should be noted that another method of obtaining 2-hydroxy-2-phenyl-1,3-dione (I) is known [2], based on the action of the equivalent of phenyl magnesium bromide on ninhydrin in a benzene solution.

On the basis of the kinetic data obtained earlier by Eskola and his co-workers during an investigation of the conversion of benzylidenephthalide to 2-phenyl-1,3-indandione by sodium alcoholate [3, 4], the initial stage of the process in question is evidently the addition of sodium methylate at the carbonyl group of dibromobenzalphthalide (II) and the formation of an intermediate compound ($Va \rightleftharpoons VIa$).

Subsequent removal of a bromine ion gives the methyl ester of α -bromodesoxybenzoin-o-carboxylic acid (VIIa), which was precipitated directly from the reaction solution; its structure was proven by reverse synthesis, i.e., by direct bromination of the methyl ester of desoxybenzoin-o-carboxylic acid [5].

The ester (VIIa) may be present in equilibrium with the tautomeric form (VIIIa), the conversions of which determine the subsequent directions of the process. If, in the case of monobromide (VIIIa) the bromine atom is first replaced by a hydroxy group, and CH_3OH is then removed, 2-hydroxy-2-phenyl-1,3-indandione (I) is formed. But if CH_3OH is first removed, 2-bromo-2-phenyl-1,3-indandione (IX) is formed. The latter contains a very active bromine atom and therefore, as was shown by the author, it can brominate the still unchanged methyl ester (VIIa), with formation of the previously unknown methyl ester of α, α -dibromodesoxybenzoin-o-carboxylic acid (Xa); 2-bromo-2-phenyl-1,3-indandione (IX) is converted during this process to 2-phenyl-1,3-indandione (III). It should be noted that as a result of the action of sodium methylate, 2-bromo-2-phenyl-1,3-indandione (IX) may be partially reconverted to the monobromo derivative (VIIIa). Finally, as a result of the action of dilute alkali the ester of α, α -dibromodesoxybenzoin-o-carboxylic acid (Xa) obtained is converted to o-carboxybenzil (IV).

The fact that these two processes take place simultaneously, leads, under Gabriel's conditions [1] to the formation of considerable amounts of 2-phenyl-1,3-indandione (III) and o-carboxybenzil (IV) together with small amounts of 2-hydroxy-2-phenyl-1,3-indandione. It was found that such secondary processes may be eliminated if dibromobenzalphthalide (II) is acted on by a 2.5% aqueous-dioxan solution of alkali instead of an alcoholic solution of sodium methylate. Under these conditions the reaction is completed in 5-10 minutes and the yield of 2-hydroxy-2-phenyl-1,3-indandione (I) is increased to 65%. The mechanism of its conversion is evidently similar to that considered above ($II \rightarrow Vb \rightarrow VIIb \rightarrow VIIIb \rightarrow I$), but here, replacement of the bromine of the intermediate compound ($VIIb \rightleftharpoons VIIIb$) by hydroxyl takes place far more rapidly than its conversion to 2-bromo-2-phenyl-1,3-indandione (IX). Since the latter is not formed here, the secondary processes observed under Gabriel's conditions are also eliminated.

The correctness of this theory is corroborated by the fact that when alkali acts on an aqueous-dioxane solution of the methyl ester of α -bromodesoxybenzoin-o-carboxylic acid (VIIa), a 70% yield of 2-hydroxy-2-phenyl-1,3-indandione (I) is obtained, whereas under these conditions 2-bromo-2-phenyl-1,3-indandione (IX) is converted almost quantitatively to 2-phenyl-1,3-indandione (III) and o-carboxybenzil (IV).

Therefore the modifications of the reaction conditions evidently did not change the mechanism of the formation of 2-hydroxy-2-phenyl-1,3-indandione from dibromobenzalphthalide (II), but they had an important effect on the capacity of intermediate compounds of the type ($VII \rightleftharpoons VIII$) to undergo conversion to 2-bromo-2-phenylindandione (IX), which made it possible to eliminate the formation of secondary products (III) and (IV).

Moreover, it was found that the best method of obtaining 2-hydroxy-2-phenyl-1,3-indandione (I) is the action of alkali on an aqueous-dioxan solution of 2-chloro-2-phenyl-1,3-indandione (XI), which is readily available [5, 6]. In this case an ordinary substitution reaction uncomplicated by secondary processes takes place, as a result of which, compound (I) is formed, the yield reaching 90%.

EXPERIMENTAL

2-Hydroxy-2-phenyl-1,3-indandione (I). 5 g of dibromobenzalphthalide (II)* was added to 100 ml of a 2% solution of sodium methylate cooled to 0°. After 30 minutes 150 ml of ice water was added to the orange-red solution and carbon dioxide was passed through the solution for 3 hours at 0-2°. The precipitated 2-hydroxy-2-phenyl-1,3-indandione (I) was filtered, washed with cold and then with hot water, recrystallized from alcohol in a current of inert gas and dried immediately under vacuum at 70°. The weight was 0.6 g (20%); the m.p. was 190-192°. **

* Dibromobenzalphthalide is obtained by bromination of benzalphthalide [7] in a chloroform solution in the cold [8].

** In this and all the other experiments the melting point of 2-hydroxy-2-phenyl-1,3-indandione (I) was determined in accordance with Gabriel's recommendation [1], i.e., under vacuum at 3-5 mm, because unless a vacuum is used it melts in the 150-155° range, i.e., with an indefinite melting point.

The main mother liquor which remained after substance (I) had been separated was diluted with 200 ml of water, acidified with 40 ml of 10% sulfuric acid and the precipitate of 2-phenylindandione was filtered. The weight was 0.9 g (31%); the m.p. was 146° (from alcohol) [5].

The mother liquor obtained was evaporated at 40-45° to 50-70 ml, cooled to 0° and the precipitate of o-carboxybenzil (IV) was filtered. The weight was 1.1 g (33%); the m.p. was 140-141° (from 50% alcohol) [9, 10].

Methyl ester of α -bromodesoxybenzoin-o-carboxylic acid (VIIa). a) The action of sodium methylate on dibromobenzaldehyde (II). 5 g of dibromobenzaldehyde was added to 100 ml of a 2% solution of sodium methylate cooled to 0°. After the mixture had been allowed to stand for 30 minutes at 0° all the dibromobenzaldehyde had gone into solution. A small seeding for ester (VIIa) was added and with rubbing with a rod this ester separated as a colorless precipitate, which was filtered. The weight was 0.5 g; the m.p. was 173° (from alcohol). 25 ml of a 5% solution of sulphuric acid in methanol was added, followed by 500 ml of water. The yellow solution obtained was extracted 5 times with ether and the ethereal solution was washed several times with a 3% soda solution and water. After it had been dried with sodium sulfate and the ether had been removed, a seeding of ester (VIIa) was added to the oily residue and the crystalline precipitate formed was washed with CCl_4 . We obtained 0.9 g of the substance, with a m.p. of 172-173° (from alcohol). The total yield of ester (VIIa) was 32%.

Found %: C 57.42; H 3.67; Br 23.81. $\text{C}_{16}\text{H}_{13}\text{O}_3\text{Br}$. Calculated %: C 57.66; H 3.90; Br 24.02.

b) Bromination of the methyl ester of desoxybenzoin-o-carboxylic acid. 5 g of the methyl ester of desoxybenzoin-o-carboxylic acid [5] was dissolved in 200 ml of ether and 8 g of bromine in 20 ml of ether was added to the solution obtained. After 2 days, when all the ether had evaporated, the residue was stirred up with 30 ml of water, filtered and washed repeatedly with water until the reaction to Congo was no longer acid. After recrystallization from methyl alcohol, 4.8 g (72%) of ester (VIIa) with an m.p. of 172-173° was obtained. A mixed melt of the substance with the compound obtained above showed no depression of the melting point.

Methyl ester of α,α -dibromodesoxybenzoin-o-carboxylic acid (Xa). a) The action of sodium methylate on the methyl ester of α -bromodesoxybenzoin-o-carboxylic acid (VIIa). 2 g of ester (VIIa) in 50 ml of methyl alcohol was added to 50 ml of a 2% solution of sodium methylate in methyl alcohol cooled to 0°. After 30 minutes, 150 ml of water was added to the bright-red solution, a current of CO_2 was passed for 3 hours and the precipitate of ester (Xa) was filtered. The weight was 0.6 g (24%); the m.p. was 183° (from acetic acid).

Found %: C 46.90; H 2.95; Br 38.95. $\text{C}_{16}\text{H}_{12}\text{O}_3\text{Br}_2$. Calculated %: C 46.60; H 2.91; Br 38.83.

2-Phenyl-1,3-indandione (II) was precipitated from the mother liquor when it was acidified with 10% sulfuric acid. The weight was 0.6 g (45%); the m.p. was 145° (from alcohol) [5].

b) The action of sodium methylate on 2-bromo-2-phenyl-1,3-indandione (IX). 5 g of indandione (IX) [5] was dissolved in 100 ml of a 2% solution of sodium methylate cooled to 0°. Precipitation of ester (Xa) commenced after 5-7 minutes and it was filtered after 30 minutes. The weight was 2.8 g (41%); the m.p. was 183° (from acetic acid). 150 ml of water and 30 ml of sulfuric acid were added to the mother liquor. The precipitated 2-phenyl-1,3-indandione (II) was filtered. The weight was 1.6 g (43%), the m.p. was 146° (from alcohol) [5].

The action of aqueous alkali on the methyl ester of α,α -dibromodesoxybenzoin-o-carboxylic acid. 0.2 g of ester (Xa) was dissolved in 30 ml of alcohol, 10 ml of a 0.25 N aqueous solution of caustic soda was added and the mixture was left to stand for 3 hours. It was then acidified with 30 ml of a 0.1 N solution of sulfuric acid and extracted with ether. We obtained 0.1 g (85%) of o-carboxybenzil (IV) with a m.p. of 140-141° (from water) [9, 10].

Determination of the oxidizing capacity of bromine in 2-bromo-2-phenyl-1,3-indandione (IX). 0.4 g of indandione (IX) was dissolved in 20 ml of glacial acetic acid, 0.5 g of potassium iodide was added; the mixture was heated for 15 minutes at 90°, 30 ml of water was added to the solution and the iodine precipitated was back-titrated with 0.1 N hyposulfite. 98.7% of iodine was found. When the titration had been completed, 2-phenyl-1,3-indandione (III) with a m.p. of 145-146° (from alcohol [5]) was precipitated from the reaction solution; the yield was 90%;

2-Hydroxy-2-phenyl-1,3-indandione (I). The action of an aqueous-dioxane solution of alkali. a) On dibromobenzaldehyde (II). 3 g of phthalide (II) was dissolved in 60 ml of dioxane and the solution was cooled to 10°; 1.8 g of caustic soda in 45 ml of water and 30 ml of dioxane were then added to the solution (cooled to 0°). After 5 minutes the reaction mixture was filtered into a receiver containing 25 ml of 10% sulfuric acid, cooled to 0°. The precipitate of 2-hydroxy-2-phenyl-1,3-indandione (I) was filtered and washed, first with cold, and then with hot water. The weight was 1.2 g (64%); the m.p. was 191° (from alcohol).

b) On the methyl ester of α -bromodesoxybenzoic acid (VIIa). 3 g of ester (VIIa) was dissolved in 100 ml of dioxane, the solution was cooled to 10° and 5.4 g of caustic soda in 140 ml of water and 90 ml of dioxane were added to the solution cooled to 0-2°. After 5 minutes the reaction solution was filtered into a receiver containing 75 ml of 10% sulfuric acid, cooled to 0°. The precipitate of 2-hydroxy-2-phenyl-1,3-indandione (I) obtained was washed with water. The weight was 1.5 g (70%); the m.p. was 190-191° (from alcohol).

c) On 2-chloro-2-phenyl-1,3-indandione (XI)*. A solution (cooled to 10°) of 3 g of 2-chloro-2-phenyl-1,3-indandione in 30 ml of dioxane was added to a solution (cooled to 0-2°) of 1.8 g of caustic soda in 90 ml of water and 30 ml of dioxane. After 5 minutes the solution was filtered into a receiver containing 25 ml of 10% sulfuric acid cooled to 0°. The precipitated 2-hydroxy-2-phenyl-1,3-indandione (I) was filtered and washed, first with cold water and then with hot. The weight was 2.5 g (90%); the m.p. was 192-193° (from alcohol).

The action of an aqueous-dioxane solution of alkali on 2-bromo-2-phenyl-1,3-indandione (IX). 3 g of indandione (IX) was dissolved in 100 ml of dioxane and the solution was acted on by an aqueous-dioxane solution of alkali under the conditions of the preceding experiment. After the reaction mixture had been acidified it was evaporated under vacuum in an atmosphere of nitrogen to about 100 ml, cooled, and the precipitated 2-phenyl-1,3-indandione (III) was filtered. The weight was 0.9 g (41%). After the mother liquor had been evaporated to 25-30 ml we obtained 1.0 g of o-carboxybenzil (IV) (39%) with an m.p. of 140-141° (from water) [9, 10].

The action of an aqueous-dioxane solution of alkali on an equimolecular mixture of 2-bromo-2-phenyl-1,3-indandione (IX) and the methyl ester of α -bromodesoxybenzoic acid (VIIa). A solution (cooled to 10°) of 3 g of bromide (IX) and 3.3 g of ester (VIIa) in 100 ml of dioxane was added to a solution of 5.4 g of caustic soda in 135 ml of water and 70 ml of dioxane, cooled to 0°. After 5 minutes the reaction mixture was acidified with 75 ml of 10% sulfuric acid, cooled to 0°. Subsequent treatment was similar to that of the above-mentioned experiment. We obtained 1.9 g (86%) of 2-phenyl-1,3-indandione (III) with an m.p. of 143-145° (from alcohol) and 2.1 g (82%) of o-carboxybenzil (IV) with an m.p. of 140-141° (from water).

SUMMARY

The mechanism of the formation of 2-phenyl-2-hydroxy-1,3-indandione from dibromobenzaldehyde was investigated and the conditions for preparing this compound were improved. It was shown that 2-phenyl-2-hydroxyindan is obtained more simply and with a higher yield (90%) from 2-chloro-2-phenyl-1,3-indandione.

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* 2-Chloro-2-phenyl-1,3-indandione (XI) was obtained with a 90% yield by passing chlorine into a solution of 2-phenyl-1,3-indandione (III) in a 1% solution of alkali (see [11]).

STEREOCHEMICAL INVESTIGATIONS

XI. AMIDES OF OPTICALLY ACTIVE α -PHENYLETHYLAMINE WITH SUBSTITUTED BENZOIC ACIDS

V. M. Potapov, V. M. Dem'yanovich, and A. P. Terent'ev

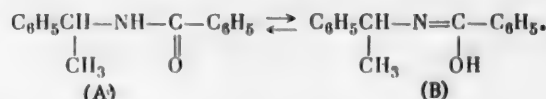
M. V. Lomonosov Moscow State University

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pp. 3046-3050, September, 1961

Original article submitted October 7, 1960

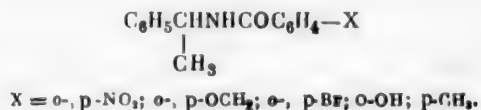
As previously reported [1, 2] by means of a spectropolarimeter our laboratory obtained data which were interpreted from the aspect of the possible existence of N-benzoyl- α -phenylethylamine in two tautomeric forms: amide (A) and imino (B), the position of the equilibrium between these forms depending on the solvent:



Some properties of amides of α -phenylethylamine with p-substituted benzoic acids were investigated by Nerdel and his co-workers [3]; on the basis of data obtained during measurement of the dipole moments in various solvents, and of ultraviolet and infrared spectra, they concluded that a chain formation of amides takes place in C_6H_6 and CHCl_3 : $\text{>N-H} \cdots \text{O}=\text{C}<$, whereas solvation of the NH group and the oxygen of the solvent takes place in dioxane and in acetone. Comparing these data with the variation in the value of optical rotation (for the 656-475 μ region) in different solvents in relation to the concentration, Nerdel concluded that the optical rotation depends on the degree of association of the optically active substance. However, if Nerdel's data on the concentration relation of the rotation value are examined, it is seen that in benzene solutions M has a negative sign and its absolute value increases with a reduction in the concentration. Therefore with a reduction in concentration, which must be accompanied by decomposition of the associated molecules, there is a discrepancy between the rotation value and the rotation observed for solutions in polar solvents (where, according to Nerdel, the investigated amides are monomeric) and, vice versa, the discrepancy between the rotation value in benzene solutions and in solutions of other solvents increases. Therefore it is found that in a very dilute benzene solution a monomeric molecule of amide has a marked (-) rotation, whereas in methanol, for example, a monomeric molecule of the same amide exhibits marked dextro rotation. In the latter case the molecules of the amide are solvated, but this can hardly be the principal cause of the change in the sign of rotation. In the light of the above, the previous assumption that tautomerism is the cause of the difference in the character of the rotation dispersion curve in different solvents appears more probable.

To make a further check of the correctness of this assumption regarding the tautomerism of amides of α -phenylethylamine, we turned our attention to the problem of the influence of the position of the substituent in the benzene ring of the acid part of the amide on the optical activity.

For this purpose we synthesized the following compounds and investigated them by means of the spectropolarimeter:



It was found that for amides with a substituent in the para position in benzene, the sign of rotation and the nature of the dispersion of the initial amine are retained. In polar solvents - methanol, chloroform, pyridine and dimethyl formamide - and also in dioxane the path of the curve is inverse. Figs. 1 and 2 give the dispersion curves

of the optical rotation, characteristic of *p*-substituted amides of α -phenylethylamine. If we assume that amide-imino tautomerism is possible for these compounds, the amide form (A) must predominate in benzene solutions, while

in all other solvents the imino form (B) is predominant. However, here we did not observe two crystalline forms, as in the case of benzoyl- α -phenylethylamine: recrystallization from various solvents - methanol, benzene, heptane - always gave substances with the same melting point. In the solid form these compounds are true amides, which is indicated by data of the infrared spectrum of *p*-nitrobenzoyl- α -phenylethylamine (in vaseline oil), in which there is a very strong absorption band in the C=O valence vibration region (1644 cm^{-1}), and also absorption corresponding to NH valence vibrations ($3274, 3354\text{ cm}^{-1}$). We only succeeded in obtaining two crystalline forms in the case of *N*-(2,5-dinitrobenzoyl)- α -phenylethylamine (m.p. $141-142^\circ$ from a mixture of CH_3OH and H_2O ; m.p. $162-163^\circ$ from C_6H_6); similar data will be given in the next communication.

In the case of amides with substituents in the ortho position (except for *o*-methoxybenzoyl- α -phenylethylamine) the sign of rotation and the path of the curves remained the same as for the initial amine (see Fig. 1 for *o*-bromobenzoyl- α -phenylethylamine). This "anomalous" behavior of ortho-substituted benzoyl- α -phenylethylamine is not unexpected because in all cases investigated hitherto [4] the character of the rotation of Schiff's bases from α -phenylethylamine and ortho-substituted benzaldehydes was unusual and different from para compounds. The disturbance of the symmetry by an ortho substituent evidently has such a marked effect on the optical rotation that in the case of ortho derivatives this effect masks the finer distinction of tautomeric structures.

EXPERIMENTAL

Acyl chlorides of substituted benzoic acids were obtained by the standard procedure: boiling the acids with a 4-5 fold amount of SOCl_2 for 5-6 hours (heating was less than 30 minutes only in the case of *o*-methoxybenzoic acid), the excess SOCl_2 was distilled and the acyl chloride was used without further purification.

3.1 g of (-) α -phenylethylamine ($[\alpha]_D^{20} -40.4^\circ$), 4.7 g of *p*-nitrobenzoyl chloride and 1.5 g of crystalline soda in 50 ml of benzene were heated on the water bath for 1 hour; the precipitated amide was filtered and recrystallized from 50% methanol; the m.p. was $141.5-142.5^\circ$. After recrystallization from benzene and from heptane the melting point of the substance was unchanged.

All the other amides were obtained in the same way (Table 1).

Spectropolarimetric measurements were carried out in a photoelectric spectropolarimeter in the 589-290 $\text{m}\mu$ wavelength region; the limit of measurements in the ultraviolet region of the spectrum depended on the absorption of the substance, which was determined by data of the ultraviolet spectrum. Tubes of length 2.1 and 0.5 inches were used in the visible part of the spectrum, and 0.2, 0.1 and 0.05 inches in the ultraviolet part (Tables 2-4).

SUMMARY

Amides of optically active α -phenylethylamine of para- and orthosubstituted benzoic acids were synthesized.

A spectropolarimetric investigation of *p*-substituted amides showed that the solvent has an effect on the character of the dispersion curves, similar to that discovered in the case of *N*-benzoyl- α -phenylethylamine.

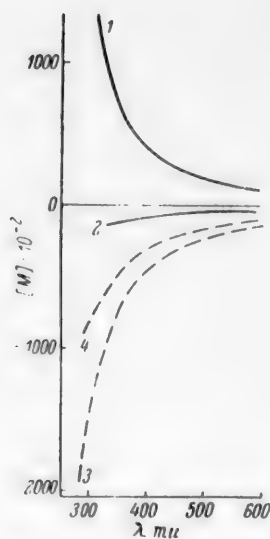


Fig. 1. Dispersion curves of molecular optical rotation: *N*-(*p*-bromobenzoyl)- α -phenylethylamine in CH_3OH (1), in C_6H_6 (2); *N*-(*o*-bromobenzoyl)- α -phenylethylamine in CH_3OH (3), in C_6H_6 (4).

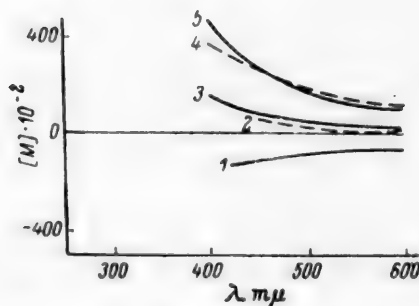


Fig. 2. Dispersion curves of the molecular optical rotation of *N*-(*p*-nitrobenzoyl)- α -phenylethylamine: 1) in C_6H_6 ; 2) in CHCl_3 ; 3) in dioxane; 4) in pyridine; 5) in CH_3OH .

TABLE 1. Amides of (-) α -Phenylethylamine $C_6H_5CH(CH_3)NHCOC_6H_4-X$

X	M.p.		Empirical formula	% N		Ultraviolet spectrum in CH_3OH	
	Found	Literature data		Found	Literature data	λ max.	log ϵ
p-NO ₂	141.5–142.5 ^o	140 ^o	C ₁₅ H ₁₄ O ₃ N ₂	—	—	265	4.16
o-NO ₂	161.5–162	—	C ₁₅ H ₁₄ O ₃ N ₂	10.62, 10.69	10.37	252	3.80
p-CH ₃	136.5–137.5	137	C ₁₆ H ₁₇ O ₂ N	—	—	235	4.20
p-OCH ₃	153.5–154.5	154.5–155	C ₁₆ H ₁₇ O ₂ N	—	—	251	4.27
o-OCH ₃	74–76	—	C ₁₆ H ₁₇ O ₂ N	5.66, 5.60	5.49	235	4.06
o-OH	109–110	—	C ₁₅ H ₁₅ O ₂ N	5.86, 5.91	5.85	287	3.54
p-Br	169–170.5	—	C ₁₅ H ₁₄ ONBr	4.78, 4.62	4.65	300	3.68
o-Br	118–119	—	C ₁₅ H ₁₄ ONBr	4.79, 4.75	4.65	240	4.20
						276	2.58
						(in C ₆ H ₆)	

TABLE 2. Molecular Rotation of N-(p-Nitrobenzoyl)- α -phenylethylamine


Solvent C*	CH ₃ OH 1.535	Dioxane 0.749	CHCl ₃ 1.195	C ₆ H ₅ N 1.559	Aqueous C ₅ H ₅ N	C ₆ H ₆ 0.687
λ						
589	+111	+26.4	+13.8	+112	+119	— 63.1
578	115	27.9	14.6	117	123	— 65.4
546	134	34.9	19.8	134	146	— 72.2
493	188	51.6	35.9	185	204	— 87.0
460	242	70.4	51.5	237	242	— 96.0
436	312	94.5	—	286	322	— 104
405	435	143	—	357	401	—

* C—concentration in grams per 100 ml of solution.

TABLE 3. Molecular Rotation of $C_6H_5CHNHCOC_6H_4-X$

X	CH ₃				OCH ₃			Br	
	CH ₃ OH 1.200	Dioxane 1.237	DMF* 1.069	C ₆ H ₆ 1.011	CH ₃ OH 1.033	Dioxane 1.215	C ₆ H ₆ 0.713	CH ₃ OH 1.334	C ₆ H ₆ 0.853
λ									
589	+81.8	+16.2	+172	— 69.3	+144	+38.4	—42.1	+116	— 58.0
578	86.8	16.3	178	— 74.4	145	39.9	—50.1	227	— 44.0
546	101	18.8	203	— 92.0	166	47.2	—50.1	145	— 47.0
493	136	27.0	268	—103	229	68.3	—60.4	—	— 70.0
436	211	43.0	387	—141	349	114	—74.5	291	— 83.0
405	286	60.2	495	—168	479	155	—74.5	374	— 83.0
365	438	100	722	—230	714	239	—83.2	570	—110
334	708	179	1134	—284	1360	436	—	896	—
313	1105	298	1525	—322	2195	750	—	1260	—
302	1500	394	1960	—333	2770	1064	—	—	—
297	1770	411	2230	—	3220	1290	—	—	—
294	1795	430	—	—	3360	—	—	—	—
293	1802	—	—	—	3410	—	—	—	—

* DMF—dimethyl formamide.

TABLE 4. Molecular Rotation of $C_6H_5CHNHCO$ 

X	OH			OCH ₃		Br		NO ₂		
	Solvent	Dioxane	C ₆ H ₆	CH ₃ OH	C ₆ H ₆	CH ₃ OH	C ₆ H ₆	CH ₃ OH	Dioxane	C ₆ H ₆
C	1.349	1.230	0.934	1.172	1.389	1.345	1.334	1.574	1.064	0.259
λ										
589	+23.9	-49.4	-167	+56.4	+24.0	-162	-113	-149.5	-62.3	-216
578	25.9	-50.0	-175	63.0	27.7	-165	-113	-157	-68.0	-230
546	26.8	-61.0	-206	79.2	34.6	-193	-131	-177	-75.2	-260
492	29.8	-93.8	—	—	—	—	—	-241	-89.0	-356
460	—	—	—	—	—	—	—	—	-95.6	-450
436	34.65	-173	-470	192	102	-358	-238	-363	—	-540
405	-41.5	-275	-677	280	161.5	-453	-298	-519	—	-698
385	-114	-401	—	—	—	—	—	-662	—	—
365	-256	-630	-1310	560	358	-632	-409	-1180	—	—
354	-400	-827	-1620	—	—	—	—	—	—	—
349	-535	-955	-1750	—	—	—	-475	—	—	—
343	-590	-1059	—	—	—	—	—	—	—	—
334	—	—	—	1310	870	-869	-560	—	—	—
313	—	—	—	3100	2290	-1200	-715	-1200	—	—
310	—	—	—	—	2480	—	—	—	—	—
302	—	—	—	—	—	-1410	-733	—	—	—
293	—	—	—	—	—	-1570	—	—	—	—
289	—	—	—	—	—	-1820	—	—	—	—

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o-AMINOPHENYLVINYL AND p-AMINOPHENYLVINYL ETHERS

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Original article submitted October 7, 1960

M. F. Shostakovskii and I. A. Chekulaeva [1] obtained vinyl ethers of ethanolamines. They established that acetylene is added only to the hydroxyl groups of diethanolamine. However, diaryl amines [2] and acridone [3] are vinylated at the imino group.

The presence of a hydroxyl and amino group in aminophenols makes it possible for two vinyl groups to become attached. Experiments showed that the products formed are o-aminophenylvinyl and p-aminophenylvinyl ether.

The structure of the vinyl ethers was proven by hydrogenation to the saturated aminophenylethyl ethers described in the literature [4].

EXPERIMENTAL

o-Aminophenylvinyl ether. 33 g of o-aminophenol, 6 g of powdered caustic potash, 300 ml of dioxane and 66 ml of water were placed in a liter rotary autoclave. The acetylene pressure at saturation was 11 atm, the temperature was 150-155°, the reaction time was 3 hours. 15.4 g (37.65% yield) of o-aminophenylvinyl ether was obtained from the reaction mixture; it decolorized bromine and an aqueous solution of permanganate.

B.p. 87.5-88.5° (10 mm), d_4^{20} 1.0975, n_D^{20} 1.5706, M_{RD} 40.4; calc. 40.4.

Found %: N 10.36, 10.4. M 135.1. C_8H_9ON . Calculated %: N 10.364. M 135.1.

Under the influence of the ether of boron fluoride, o-aminophenylvinyl ether polymerized on cooling to a solid reddish product, readily soluble in dioxane, acetone, and methanol. The softening point was 90-95°, the decomp. temp. was 115-120°. M was 8090, the degree of polymerization was 60.

Under similar conditions, o-aminophenylvinyl ether copolymerized with vinylbutyl ether (1 : 1) to a viscous product with a molecular weight of 7040. The copolymer dissolved in ether, methanol, acetone, dioxane, styrene, toluene and chloroform.

o-Aminophenylethyl ether. 7.7 g of aminophenylvinyl ether was hydrogenated over 0.5 g of Raney nickel in 15 ml of alcohol. After the catalyst and the solvent had been removed and the material had been distilled, we obtained 4.8 g (61.3%) of o-aminophenylethyl ether with an m.p. of 226°, n_D^{20} 1.555. According to [4], the b.p. is 228°.

Found: M 138. Calculated: M 137.1.

p-Aminophenylvinyl ether. The initial substances and conditions were similar to the synthesis of o-aminophenylvinyl ether.

23.5 g (57.5% yield) of p-aminophenylvinyl ether with a b.p. of 103-104° (10 mm) was obtained from the reaction mixture; it decolorized bromine and an aqueous solution of permanganate.

B.p. 103-104° (10 mm), d_4^{20} 1.080, n_D^{20} 1.5788, M_{RD} 41.4; calc. 40.4.

Found %: N 10.33, 10.38. M 135.1. C_8H_9ON . Calculated %: N 10.364. M 135.1.

Under the influence of the ether of boron fluoride, p-aminophenylvinyl ether polymerized on cooling to a solid, weakly acid product, readily soluble in dioxane, acetone and methanol. The softening point was 85-90°, the decomp. temp. was 120°, M was 10110, the degree of polymerization was 75.

p-Aminophenylvinyl ether was copolymerized with vinylbutyl ether (1 : 1) to a viscous product with a molecular weight of 6570. The copolymer dissolved in ether, methanol, acetone, dioxane and chloroform.

p-Aminophenylethyl ether. The experiment was carried out in the same way as the reduction of o-amino-phenylvinyl ether. The constants of the p-aminophenylethyl ether obtained in this way corresponded to literature data [4].

SUMMARY

1. o-Aminophenylvinyl and p-aminophenylvinyl ether were synthesized from acetylene and o- or p-amino-phenol.
2. The ethers obtained polymerize; they copolymerize with vinylbutyl ether, solid and viscous products being obtained.

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PREPARATION OF AMINOALKYL ESTERS OF BENZILIC ACID

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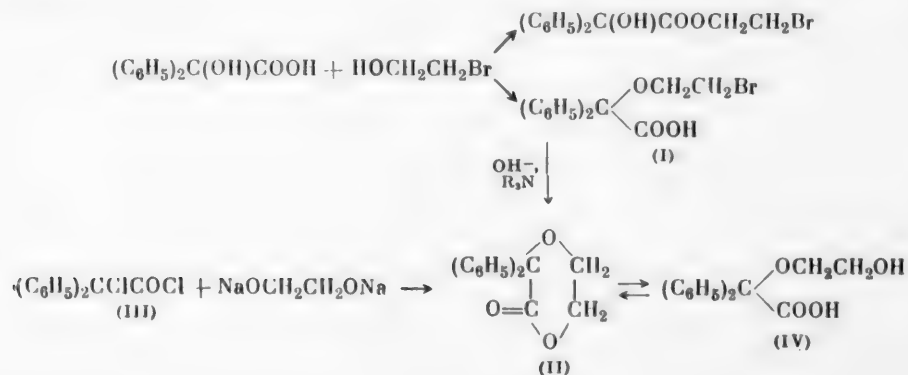
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The reaction of ω -alkyl halide esters of acids with amines is a convenient method of synthesizing amino-alkyl esters of various acids [1-3]. In some cases this method is not merely convenient, but is the only way in which such esters may be obtained. The synthesis of alkyl-(δ -hydroxybutyl)-aminoethyl esters of diphenylacetic acid from N-alkyl aminobutalones and the 2-bromoethyl ester of diphenylacetic acid, described by the authors [4], may serve as an example. However, when attempts were made to obtain similar esters of benzilic acid in the same way we met a number of difficulties in preparing the intermediate products, which necessitated a more detailed investigation of this method of synthesis.

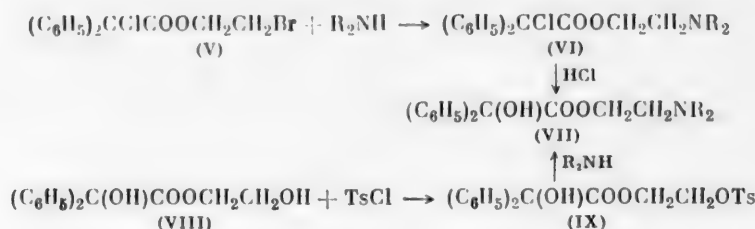
The 2-bromoethyl ester of benzilic acid was obtained earlier by reacting benzilic acid with an excess of ethylene bromhydrin in carbon tetrachloride in the presence of a small amount of sulfuric acid [2]. However, when this synthesis was repeated we obtained α -(2-bromoethoxy)-diphenylacetic acid (I) as the main product, together with a small amount of the 2-bromoethyl ester of benzilic acid. The high mobility of the tertiary hydroxyl in benzilic acid, particularly in the presence of strong acids, is well known [5]. The ease with which ethers of compounds containing a diphenylmethylol group, for example benzhydrol, are formed is also known [6]. In the case in question, the fact of the preferential formation of an ether, and not an ester, is of interest. The reason for this lies both in the high mobility of the tertiary hydroxyl of the acid and in the somewhat greater acidity of ethylene bromhydrin compared with ordinary alcohols, which when reacted with benzilic acid under similar conditions give esters. The ratio between ethers and esters varies to some extent in relation to the amount of ethylene bromhydrin. An increase in the excess of the latter leads to the formation of a large amount of ester the yield of which reaches 38% in the presence of a four-fold excess of alcohol. But the use of a still larger excess of alcohol leads to the formation of an etherification product at the carboxyl and hydroxyl groups simultaneously [2]

If the ease with which an ether is formed is due to the acidity of the alcohol, it may be assumed that other halohydrins will react in a similar way to ethylene bromhydrin. In fact, when benzilic acid was reacted with ethylene chlorhydrin and ethylene iodohydrin, the principal reaction products were the corresponding α -(2-haloethoxy)-diphenylacetic acids. All three α -(2-haloethoxy)-diphenylacetic acids obtained react readily with bases, splitting off a molecule of hydrogen halide and forming the lactone of α -(2-hydroxyethoxy)-diphenylacetic acid, i.e., 3,3-diphenyl-2-oxo-1,4 dioxane (II). To prove the structure, we obtained the latter by reacting the acyl chloride of diphenylchloroacetic acid (III) with the disodium derivative of ethylene glycol, i.e., by the method usually employed for the synthesis of derivatives of 2-oxo-1,4 dioxane [7,8].



When the lactone was reacted with an equivalent amount of alkali the disodium salt of α -(2-hydroxyethoxy)-diphenylacetic acid was obtained, careful acidification of an aqueous solution of this salt giving the acid (IV) itself. The latter is a very labile compound and is already lactonized on recrystallization. The acid is characterized in the form of the *p*-nitrobenzyl ester.

Therefore the properties of benzoic acid containing an active tertiary hydroxyl were an obstacle to obtaining the 2-bromoethyl ester. To obtain aminoethyl esters of benzoic acid we therefore employed the 2-bromoethyl ester of diphenylchloroacetic acid instead of the benzoic ester. It is known that the halogen in α -halogendiphenylacetic acids and their derivatives has a low activity in reactions with amines, particularly in an inert solvent [9, 10]. This is evidently due to the marked steric hindrance caused by the two phenyl rings. On the other hand, when heated with dilute acids the halogen in the α -position is readily replaced by a hydroxy group [11]. It was to be expected that when diphenylchloroacetic acid 2-bromoethyl ester (V) reacts with a dialkyl amine with subsequent hydrolytic removal of the chlorine in the resulting diphenyl chloroacetic acid amino ester (VI), benzoic acid aminoethyl esters (VII) may be formed. In point of fact the required esters were obtained with 50% yields.



The essential shortcoming of this method is the difficulty of purifying the intermediate aminoesters of diphenylchloroacetic acid, as a result of which we purified only the end products. The impurities formed made such purification difficult to some extent and led to appreciable losses of the required compounds. We therefore developed another method of synthesizing aminoethyl esters of benzoic acid. For the initial compound we used our synthesized benzoic acid 2-hydroxyethyl ester (VIII), formed with a high yield by reacting benzoic acid and ethylene glycol in the presence of sulfuric acid. The ester obtained was converted to the tosylate (IX), the tosyl group of which is readily replaced by an amino group, with ~70% yield. By reason of the ease with which the intermediate products are purified it may be assumed that this method is more convenient than those described above. This method was also used for the synthesis of the methyl-(δ -hydroxybutyl)-aminoethyl ester of benzoic acid required.

EXPERIMENTAL

Reaction of benzoic acid with ethylene bromhydrin. A solution of 0.05 g-mole of benzoic acid, 0.1 g-mole of ethylene bromhydrin and three drops of sulfuric acid in 75 ml of benzene were boiled in a flask (equipped with a water trap) for 5-6 hours until separation of water had ceased. 50 ml of benzene was then distilled and the precipitate of α -(2-bromoethoxy)-diphenylacetic acid which came out on cooling was separated. The yield was 12.7 g (76%), the m.p. was 143.5° (from alcohol).

Found %: C 57.42, 57.31; H 4.48, 4.45. $\text{C}_{16}\text{H}_{15}\text{O}_3\text{Br}$. Calculated %: C 57.31; H 4.51.

The filtrate obtained after separation of the precipitate was washed with a soda solution until there was no longer an acid reaction; it was then dried with calcium chloride. After the benzene had been driven off, the 2-bromoethyl ester of benzoic acid was distilled. The yield was 2.4 g (14%), the b.p. was 187-190° (2 mm). According to literature data [2], the b.p. is 173-180° (0.2 mm).

By reacting benzoic acid with ethylene chlorhydrin under similar conditions we obtained the 2-chloroethyl ester of benzoic acid (20%) with a b.p. of 178-184° (3 mm), and α -(2-chloroethoxy)-diphenylacetic acid (74%), with an m.p. of 129° (from ethyl acetate).

Found %: C 66.43, 66.32; H 4.99, 5.08. $\text{C}_{16}\text{H}_{15}\text{O}_3\text{Cl}$. Calculated %: C 66.12; H 5.19.

By reacting benzoic acid with ethylene iodohydrin we obtained α -(2-iodoethoxy)-diphenylacetic acid (91%). The m.p. was 154° (decomp. from ethyl acetate).

Found %: C 50.37, 50.57; H 4.08, 4.06. $\text{C}_{16}\text{H}_{15}\text{O}_3\text{I}$. Calculated %: C 50.30; H 3.96.

3,3-Diphenyl-2-oxo-1,4-dioxan (II). A) A solution of 0.01 g-mole of α -(2-haloethoxy)-diphenylacetic acid and an equivalent amount of amine (triethylamine, pyridine, diethanolamine) in 25 ml of benzene were boiled for 1 hour.

B) A solution of an equivalent amount of sodium ethylate was added to a solution of 0.01 g-mole of α -(2-haloethoxy)-diphenylacetic acid in 20 ml of anhydrous alcohol and the mixture was boiled for 15 minutes. The precipitated salt was separated and the benzene was distilled. The yield was quantitative, the m.p. was 98° (from alcohol).

C) A solution of 0.46 g of sodium in 10 ml of ethylene glycol was added to a solution of 2.65 g of the acyl chloride of diphenylacetic acid [12] in 15 ml of xylene and the latter was distilled for 1 hour. The residue was poured into 30 ml of water and the precipitate formed was separated. The yield was 2.1 g (82%), the m.p. was 98° (from alcohol). A mixed melt with the substances obtained by methods A and B showed no depression of the melting point.

Found %: C 75.19, 75.12; H 5.50, 5.56. $C_{16}H_{14}O_3$. Calculated %: C 75.59; H 5.55.

α -(2-Hydroxyethoxy)-diphenylacetic acid (IV). A solution of 0.03 g-at. of sodium was added to a solution of 0.03 g-mole of 3,3-diphenyl-2-oxo-1,4-dioxane in 25 ml of alcohol, and the mixture was boiled for 1 hour. The sodium salt of α -(2-hydroxyethoxy)-diphenylacetic acid which was precipitated after cooling, was separated. It was dissolved in 25 ml of water, filtered and acidified with a 3% solution of hydrochloric acid while cooling and stirring. The melting point of the acid obtained was 118-120°. When the acid was recrystallized from benzene it was partially lactonized and the melting point fell. Lactonization also took place when it was kept at room temperature. Heating in a solution of alcohol or benzene in the presence of traces of mineral acid led to immediate quantitative formation of lactone.

The p-nitrobenzilic ester of α -(2-hydroxyethoxy)-diphenylacetic acid was obtained by boiling an aqueous-alcoholic solution of equivalent amounts of the sodium salt of the acid and p-nitrobenzil bromide. The m.p. was 120° (from alcohol).

Found %: N 3.55, 3.65. $C_{23}H_{21}O_6N$. Calculated %: N 3.45.

The 2-bromoethyl ester of diphenylacetic acid (V). A mixture of 10.8 g of the acyl chloride of diphenylchloroacetic acid and 6 g of ethylene bromhydrin was heated to 120°. Vigorous liberation of hydrogen chloride commences at this temperature. The temperature of the mass rose slowly to 140° and it was heated for 2 hours. The mixture was cooled, dissolved in 30 ml of ether, washed with a soda solution and then with water; the ether solution was then dried with calcium chloride. After the ether had been driven off, the product was distilled. The yield was 14.5 g (82%).

B.p. 193-194° (3 mm), n_D^{20} 1.5917, d_4^{20} 1.4320, MR_D 83.49. $C_{16}H_{14}O_2BrCl$. Calculated: 83.39.

The hydrochloride of benzilic acid diethylaminoethyl ester. A solution of 0.005 g-mole of the 2-bromoethyl ester of diphenylchloroacetic acid and 0.01 g-mole of diethylamine in 15 ml of anhydrous benzene was boiled for 2 hours. The precipitate of diethylamine hydrobromide was separated. The yield of the latter was 0.57 g (74%), the m.p. was 210-211°. A mixed melt with the known product showed no depression of the melting point. The benzene solution was extracted with 10 ml of 1 N hydrochloric acid, charcoal was added to the acid solution and it was heated on the water bath for 40 minutes, filtered and cooled. Ammonia was added until an alkaline reaction was obtained and the oil which came out was extracted with ether. The ether solution was dried with sodium sulfate and after it had been filtered an alcoholic solution of hydrogen chloride was added. The yield of the hydrochloride of the benzilic acid diethylaminoethyl ester was 1.0 g (56%), the m.p. was 174-175° (from alcohol and acetone). A mixed melt with the known product showed no depression of the melting point.

The hydrochloride of benzilic acid dimethylaminoethyl ester was obtained in a similar way from dimethylamine and the 2-bromoethyl ester of diphenylchloroacetic acid, with a yield of 52%. The m.p. was 185°. A mixed melt with the known product showed no depression of the melting point.

Benzilic acid 2-hydroxyethyl ester (VIII). A solution of 0.15 g-mole of benzilic acid, 0.3 g-mole of ethylene glycol and 5 drops of sulfuric acid in 100 ml of benzene were boiled in a flask (equipped with a water trap) for 5-6 hours until no more water separated. The cooled solution was washed with soda and the benzene was distilled. The residue crystallized. The yield was 33.0 g (81%), the m.p. was 96° (from ethyl acetate).

Found %: C 70.72, 69.96; H 6.32, 6.38. $C_{16}H_{16}O_4$. Calculated %: C 70.53; H 5.92.

Toluenesulfonate of benzilic acid 2-hydroxyethyl ester (IX). 15 g of finely crushed potash was added to a solution of 0.1 g-mole of the 2-hydroxyethyl ester of benzilic acid and 0.1 g-mole of p-toluenesulfonyl chloride in 150 ml of acetone and the mixture was boiled with constant stirring for 6 hours. The precipitate was separated and the acetone was distilled. The residue crystallized. After crystallization from acetone the toluenesulfonate of 2-hydroxyethyl ester of benzilic acid melted at 111-113°, the yield was 26.7 g (63%).

Found %: S 7.90, 7.92. $C_{23}H_{22}O_6S$. Calculated %: S 7.52.

Benzilic acid methyl-(δ -hydroxybutyl)-aminoethyl ester. A solution of 0.005 g-mole of the toluenesulfonate of the 2-hydroxyethyl ester of benzilic acid and 0.01 g-mole of N-methylaminobutanol [4] in 10 ml of anhydrous toluene was boiled for 1 hour. The toluenesulfonic acid salt of the aminoalcohol, which came out as a viscous oil when the reaction mixture cooled, was separated and the toluene layer was washed with water. The toluene layer was then extracted several times with 5% hydrochloric acid. Ammonia was added to the acid extracts until an alkaline reaction was obtained, and the oil was extracted with benzene. The benzene extract was dried with sodium sulfate, filtered and the benzene was distilled. The residue crystallized. The yield was 1.20 g (67%), the m.p. was 70-70.5° (from alcohol).

Found %: C 70.43, 70.67; H 7.88, 7.85; N 4.13, 4.16. $C_{21}H_{27}O_4N$. Calculated %: C 70.55; H 7.61; N 3.92.

SUMMARY

1. When benzilic acid reacts with ethylene halohydrins in the presence of sulfuric acid, α -(2-haloethoxy)-diphenylacetic acids are formed together with 2-haloethoxyl esters of benzilic acid. When these diphenylacetic acids are acted on by bases, the lactone of α -(2-hydroxyethoxy)-diphenylacetic acid is formed.

2. Dialkylaminoethyl esters of benzilic acid may be obtained by reacting the 2-bromoethyl ester of diphenylchloroacetic acid with a dialkyl amine, followed by removal of the chlorine by hydrolysis. The same esters are formed by the reaction of amines with the tosyl derivatives of the 2-hydroxyethyl ester of benzilic acid.

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SYNTHESIS OF THIAZOLE DERIVATIVES

XVI. NEW HYDROXYALKYL-2-METHYLBENZTHIAZOLES

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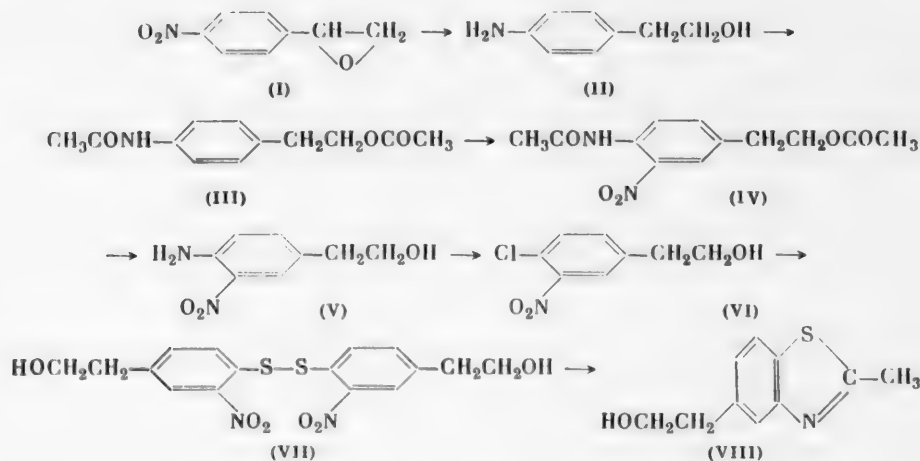
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pp. 3056-3062, September, 1961

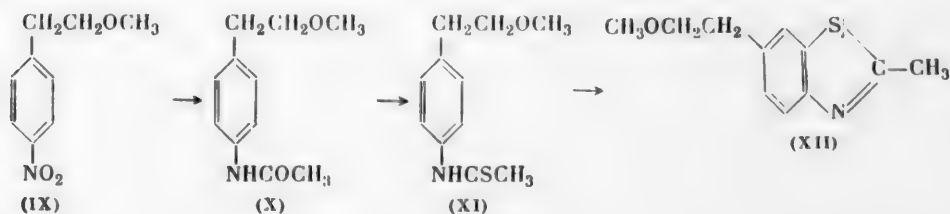
Original article submitted September 18, 1960

2-Methylbenzthiazole derivatives containing hydroxymethyl groups in the benzene ring are described in the literature [4], whereas their homologs - β -hydroxyethyl-substituted - are unknown. In the present work, 5-(β -hydroxyethyl)- and 6-(β -methoxyethyl)-2-methylbenzthiazoles (VIII and XII) were synthesized, and cyanine dyes were obtained from them. Compound (VIII) was synthesized by the method described below.

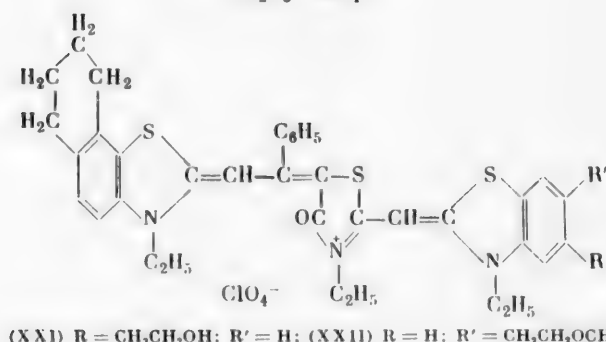
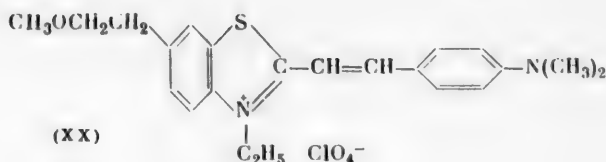
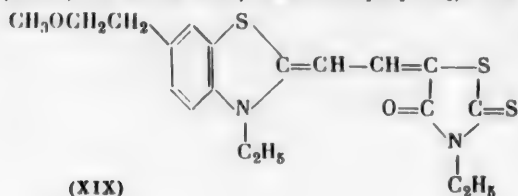
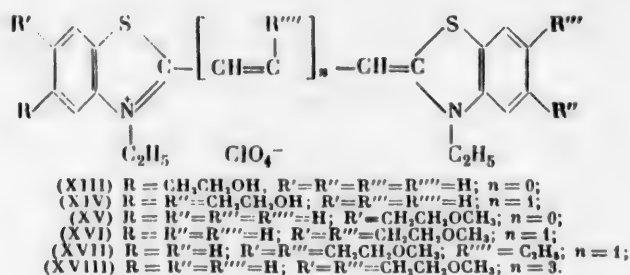
The first stage - catalytic hydrogenation of product (I) - makes it possible to prepare amine (II) relatively simply, no method for the preparation of this compound being given in the literature. Substances (I-V) are described [2], but constants and analytical data are not given for compound (V); substances (VI-VIII) were obtained for the first time. The base (VIII) is a colorless crystalline substance, similar in properties to 5-hydroxymethyl-2-methylbenzthiazole [1].



We did not succeed in converting the amine (II) to 6-(β -hydroxyethyl)-2-methylbenzthiazole by Jacobson's method. However, the methyl ester of the latter compound was synthesized by this method from the β -(p-nitrophenyl)-ethylmethyl ester:



Substances (IX -XII) were not mentioned in the literature. Bases (VIII) and (XII) were converted to the quaternary salts, from which various cyanine dyes were obtained.



The presence of β -hydroxy- or β -methoxyethyl groups in the heterocyclic radicals of cyanine dyes causes their high solubility in alcohol and water, which impedes their precipitation and purification; they were therefore precipitated as the perchlorates, the solubility of which in alcohol is nevertheless considerable.

With respect to color change, the introduction of β -hydroxyethyl groups in the 5,5' and β -methoxyethyl groups in the 6,6'-position of thiacyanine molecules is equivalent to the introduction of ethyl groups in the same positions: depending on the type of dye, it either causes no change or displaces the principal absorption maximum by only a few millimicrons in the longwave part of the spectrum.

EXPERIMENTAL

β -(p-Aminophenyl)-ethyl alcohol (II). 100 g of compound (I) [3] was dissolved in 200 g of anhydrous methyl alcohol and was hydrogenated in a 500 ml steel autoclave (equipped with a stirrer) at 50° and a pressure of 40 atm in the presence of 1.8 g of anhydrous sodium carbonate and 4 g of Raney nickel until 53.7 liters of hydrogen had been observed. The catalyst and the soda were filtered, the solvent was distilled completely from the filtrate at the pump and the light-brown viscous mass which remained (82.5 g) was extracted repeatedly with petroleum ether (b.p. 50-80°). The ether was distilled and 33 g (40%) of compound (II) with an m.p. of 105-107° (from petroleum ether) was obtained.

Found %: N 9.99, 9.85. C₈H₁₁ON. Calculated %: N 10.21.

β -(p-Acetylamino-phenyl)-ethyl acetate (III). 10 g of compound (II), 4 g of anhydrous CH_3COONa and 20 ml of acetic anhydride were boiled for 2 hours, the mixture was left to cool and was poured into a 10-fold excess of water and ice. The crystalline precipitate was washed repeatedly with water. The yield of product (III) was 16.5 g (95%); the m.p. was 95° (from 25% alcohol).

Found %: N 6.53, 6.54. $\text{C}_{12}\text{H}_{15}\text{O}_3\text{N}$. Calculated %: N 6.33.

β -(4-Acetylamino-3-nitrophenyl)-ethyl acetate (IV). 4.4 g of compound (III) was added slowly with stirring to 7.4 ml of HNO_3 (d 1.45) at $30-40^\circ$. After 20 minutes the mixture was poured onto ice, the precipitate was filtered and washed with water. The yield of the nitroproduct (IV) was 4.3 g (81%); the m.p. was 78° (from 25% alcohol).

Found %: N 10.32, 10.28. $\text{C}_{12}\text{H}_{14}\text{O}_5\text{N}_2$. Calculated %: N 10.52.

β -(4-Amino-3-nitrophenyl)-ethyl alcohol (V). A mixture of 5.0 g of compound (IV) and 40 ml of 8 N HCl was boiled for 1 hour and was treated with ammonia in the cold until an alkaline reaction was obtained. The oil which separated was extracted 4 times with ether, the extract was washed with water and dried with anhydrous Na_2SO_4 . The m.p. of compound (V) was $85-86^\circ$ (from benzene); the yield was 69.5%.

Found %: N 15.10. $\text{C}_8\text{H}_{10}\text{O}_3\text{N}_2$. Calculated %: N 15.38.

β -(3-Nitro-4-chlorophenyl)-ethyl alcohol (VI). 1.82 g of compound (V) was dissolved in 4.4 ml of HCl (d 1.14) and was diazotized at -5° with a solution of 0.7 g of NaNO_2 in 2 ml of water. The diazo solution was added slowly to a solution of 1.3 g of $\text{C}_6\text{H}_2\text{Cl}_2$ in 4.5 ml of HCl (d 1.14) at -10° , the mixture was left for 0.5 hours without cooling; it was then heated to 60° and left to cool. The oil was extracted with ether, the extract was washed with 5% aqueous K_2CO_3 and then with water until a neutral reaction was obtained; it was dried with anhydrous Na_2SO_4 and the solvent was distilled. The residue was 0.8 g of compound (VI) (75.5%); the m.p. was $48-49^\circ$ (from petroleum ether).

Found %: Cl 17.65, 17.86. $\text{C}_8\text{H}_9\text{O}_3\text{NCl}$. Calculated %: C 17.61.

Bis[4-(β -hydroxyethyl)-2-nitrophenyl]-disulfide (VII). A mixture of 0.9 g of $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$, 8 ml of methyl alcohol and 0.12 g of powdered sulfur was boiled for 0.5 hours. The solution was added dropwise for 1 hour to a boiling solution of 1.5 g of compound (VI) in 5 ml of methyl alcohol and was boiled for another hour. The solvent was driven off and the residue was treated with anhydrous ether. The disulfide (VII) consisted of yellow crystals with an m.p. of 138° (from toluene); the yield was 20%.

Found %: S 16.48, 16.49. $\text{C}_{16}\text{H}_{16}\text{O}_6\text{N}_2\text{S}_2$. Calculated %: S 16.16.

2-Methyl-5-(β -hydroxyethyl)-benzthiazole (VIII). A powdered mixture of 1.56 g of sulfide (VII) and 3.75 g of zinc dust was added at 80° in small portions over a period of 40 minutes (with stirring) to 21 ml of glacial acetic acid. The mixture was heated for 0.5 hours at 100° and 2.4 ml of acetic anhydride was added gradually. It was stirred, boiled for 2 hours, cooled and 25 ml of water was added. The zinc dust was filtered and it was washed several times with ether. A solution of 3 g of NaOH in 210 ml of water was added to the ethereal-aqueous filtrate and it was extracted with 250 ml of ether. An oil with a b.p. of $162-165^\circ$ (4 ml) came out of the extract after it had been washed with 3% NaOH and water and dried with anhydrous K_2CO_3 . The yield of compound (VIII) was 1.2 g (78%). The substance gradually hardened; the m.p. was 56° (from petroleum ether).

Found %: N 6.96, 6.85. $\text{C}_{10}\text{H}_{11}\text{ONS}$. Calculated %: N 7.25.

1.45 g of benzthiazole (VIII) and 1.6 g of the ethyl ester of p-toluenesulfonic acid were heated for 7 hours at 150° ; the quaternary salt which was formed was purified in the usual manner. The yield was 2.65 g (87%).

β -(p-Nitrophenyl)-ethylmethyl ester (IX). 13.6 g of the β -phenylethylmethyl ester was added with stirring at $15-18^\circ$ in 1.5 hours to a mixture of 24 g of H_2SO_4 (d 1.84) and 16.0 g of HNO_3 (d 1.45). Stirring at this temperature was continued for 0.5 hours and the mixture was poured onto ice. The nitro product was extracted with ether, the extract was dried with anhydrous Na_2SO_4 , the solvent was distilled, the residue (18.5 g) was kept at -10° , -15° and the para isomer was filtered; the yield was 9.7 g (54%); yellowish needles with an m.p. of $61-62^\circ$ (from petroleum ether).

Found %: N 7.79, 7.88. $\text{C}_9\text{H}_{11}\text{O}_3\text{N}$. Calculated %: N 7.73.

No.	Dye	Initial substances (g)		Solvent (ml)
(XIII)	3,3'-Diethyl-5-(β -hydroxyethyl)-thiacyanine perchlorate	A (0.4)	C (0.33)	Alcohol (4)
(XIV)	3,3'-Diethyl-5,5'-di(β -hydroxyethyl)-thiacarbocyanine perchlorate	A (0.4)	D (0.3)	Pyridine (1), acetic anhydride (1)
(XV)	3,3'-Diethyl-6-(β -methoxyethyl)-thiacyanine perchlorate	B (0.4)	C (0.35)	Alcohol (3)
(XVI)	3,3'-Diethyl-6,6'-di(β -methoxyethyl)-thiacarbocyanine perchlorate	B (0.8)	D (0.6)	Acetic anhydride (1) pyridine (2)
(XVII)	3,3',9-Triethyl-6,6'-di(β -methoxyethyl)-thiacarbocyanine perchlorate	B (0.8)	F (2.0)	Pyridine (2.0)
(XVIII)	3,3'-Diethyl-6,6'-di(β -methoxyethyl)-thiatricarbocyanine perchlorate	B (0.9)	G (0.29)	Alcohol (5)
(XIX)	3-Ethyl-5-[3'-ethyl-6'-(β -methoxyethyl)-benzthiazolidine-2-ethylidene] rhodanine	B (0.8)	H (0.6)	Pyridine (2.5)
(XX)	Ethyl perchlorate-2-(p-dimethylaminostyryl)-6-(β -methoxyethyl)-benzthiazole	B (0.4)	I (0.15)	Acetic anhydride (3)
(XXI)	3,3'-Diethyl-5'-(β -hydroxyethyl)-4-keto-5-[β -(3"-ethyl-6",7"-tetramethylene-benzothiazolinidene-2")- α -phenylethylidene]-thiazolinothiacyanine perchlorate	A (0.4)	E (0.24 ^d)	Pyridine (3), acetic anhydride (1)
(XXII)	3,3'-Diethyl-6'-(β -methoxyethyl)-4-keto-5-[β -(3"-ethyl-6",7"-tetramethylene-benzthiazolinidene-2')- α -phenylethylidene]-thiazolinothiacyanine	B (0.4)	E (0.24 ^d)	Acetic anhydride (2)

Notes: a) All the dyes were crystallized from alcohol; b) λ_{\max} were determined in alcoholic solution in a SF-2M spectrophotometer; c) the triethylamine was added dropwise to a hot mixture of the reacting substances until a blue solution was formed; d) used in the form of the quaternary salt, for the preparation of which the indicated amount of substance E was heated with 0.63 g of dimethyl sulfate for 25 minutes at 145° and the salt formed was washed with anhydrous ether; e) the crude dye, precipitated with ether, was chromatographed in chloroform on Al_2O_3 , the blue was washed out with methanol and the dye was precipitated as the perchlorate. The asterisks signify the dyes which melt with decomposition.

β -(p-Acetylamino-phenyl)-ethylmethyl ester (X). 36.2 g of compound (IX) was added in 1 hour to a solution of 150 g of $SnCl_2 \cdot 2H_2O$ in 300 ml of HCl (d 1.19). After 20 minutes, 40% NaOH was added with cooling until the tin hydroxide had dissolved. The yellow oil was extracted with 300 ml of chloroform, the extract was washed with water until there was no trace of alkali in the wash water, and it was then dried with anhydrous Na_2SO_4 . 30 g (99%) of β -(p-aminophenyl)-ethylmethyl ester was obtained from the extract and was acetylated without further purification. 40 ml of acetic anhydride was added to the amino derivative and the heated mixture was left for 0.5 hours. 150 ml of water was added and the mixture was heated until a solution was obtained. When the latter had cooled, colorless needles were precipitated and these were filtered and washed with water. The yield of compound (X) was 32.7 g (84.2%), the m.p. was 86° (from petroleum ether).

Found %: N 7.50, 7.52. $C_{11}H_{15}O_2N$. Calculated %: N 7.25.

2-Methyl-6-(β -methoxyethyl)-benzthiazole (XII). A powdered mixture of 19.3 g of compound (X) and 11.1 g of P_2S_5 was heated for 10 minutes at 120°. The melt was dissolved in 100 ml of 20% NaOH, CO_2 was passed for 0.5 hours into the filtered solution acidified with acetic acid until a white turbidity was formed, and compound (XI) was extracted with chloroform. The extract was washed with water and dried with anhydrous Na_2SO_4 , the chloroform was distilled, the residue was dissolved in 150 ml of 10% NaOH and a solution of 69 g of $K_3[Fe(CN)_6]$ in 395 ml of water was added slowly at +5° to the alkaline liquid; the mixture was left for 20 hours and was steam distilled. The distillate was extracted with 300 ml of chloroform, the extract was dried with anhydrous K_2CO_3 , the solvent was driven off and it was distilled. The yield of benzthiazole (XII) was 6.25 g (32%), calculated on the initial (X); the b.p. was 132-145° at 5 mm.

Condensing agent (ml)	Heating time (min)	Yield %	Melting point ^a	λ_{\max}^b m μ	Empirical formulae of the dyes	% Cl	
						found	calculated
N(C ₂ H ₅) ₃ (0.25)	30	68.4	222°	428	C ₂₁ H ₂₃ O ₅ N ₂ S ₂ Cl	7.37, 7.32	7.35
—	90	26.6	130	568	C ₂₅ H ₂₉ O ₄ N ₂ S ₂ Cl	6.19 7.27	6.42
N(C ₂ H ₅) ₃ ^c (0.25)	30	30.5	226	427	C ₂₂ H ₂₅ O ₅ N ₂ S ₂ Cl	7.35	7.15
—	60	45	207°	566	C ₂₇ H ₃₃ O ₆ N ₂ S ₂ Cl	5.90 6.00	6.11
Acetic anhydride (0.1)	60	27	102°	557	C ₂₉ H ₃₇ O ₆ N ₂ S ₂ Cl	5.78 5.74	5.83
Piperidine (0.3)	7	30	151°	773	C ₃₁ H ₃₇ O ₆ N ₂ S ₂ Cl	5.66 5.36	5.52
—	30	74	202	530	C ₁₉ H ₂₂ O ₂ N ₂ S ₃	N 6.83 6.75	N 6.88
—	30	34	231°	530	C ₂₂ H ₂₇ O ₅ N ₂ SCl	7.68 7.55	7.61
N(C ₄ H ₉) ₃ (0.5)	60	70.5 ^c	279	618	C ₃₈ H ₄₀ O ₆ N ₃ S ₃ Cl	4.65 4.44	4.63
N(C ₂ H ₅) ₃ (0.3)	60	20	272	619	C ₃₉ H ₄₂ O ₆ N ₃ S ₃ Cl	4.61 4.63	4.55

Found %: N 7.06, 7.00. C₁₁H₁₃ONS. Calculated %: N 6.76.

The quaternary salt was obtained from equimolecular amounts of compound (XII) and the ethyl ester of p-toluenesulfonic acid, as in the similar case of compound (IX); the yield of the salt was 75-77%.

Cyanine dyes (XIII-XXII) (Table). Known standard methods were used for the synthesis of the dyes.

The following key is adopted: A) tosylate of compound (VIII); B) tosylate of compound (XII); C) tosylate of 2-methyl mercaptobenzthiazole; D) orthoformic ester; E) 3-ethyl-5-(3'-ethyl-6',7'-tetramethylenbenzthiazolidene-2')- α -phenylethylene rhodanine; F) orthopropionic ester; G) hydrocinnamic acid salt of anililide of glutaric aldehyde; H) 3-3-ethyl-5-acetanilidomethylene rhodanine; I) p-dimethylaminobenzaldehyde.

SUMMARY

5-(β -Hydroxyethyl)- and 6-(β -methoxyethyl)-2-methylbenzthiazole were synthesized and were used for making 10 cyanine dyes, for which the principal absorption maxima were determined.

A method was proposed for obtaining p-aminophenylethyl alcohol from the oxide of p-nitrostyrene. New derivatives of phenylethyl alcohol were synthesized.

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ACYL CHLORIDE OF ISOCYANATO PHENYL PHOSPHINIC ACID

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It was previously shown that the reaction between phosphorus pentachloride and urethan takes place with liberation of 2 moles of hydrogen chloride and the formation of the ethyl ester of trichlorophosphazocarbonic acid [1], i.e., like the reaction of phosphorus pentachloride with amides of sulfonic acids [2].



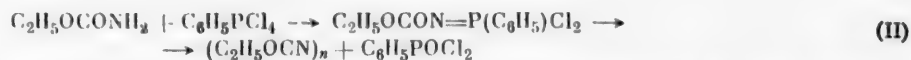
It was subsequently found that this reaction is quite general and takes place smoothly not only with amides of sulfonic acids, but also with amides of carboxylic acids [3] and even with aromatic amines [4]. Moreover, instead of phosphorus pentachloride its derivatives, in which one or more chlorine atoms are replaced by hydrocarbon radicals [5] or aroxy groups [6], may be used as the phosphorus-containing component.

To extend the limits of application of the phosphazo reaction we investigated the reaction of esters of carbamic acid with phenyl phosphorus tetrachloride. On the basis of the general character of the phosphazo reaction it could be assumed that phenyl phosphorus tetrachloride would react with ethyl urethan in the same way as with phosphorus pentachloride, i.e., with liberation of 2 moles of hydrogen chloride and formation of the ethyl ester of phenyl dichlorophosphazocarbonic acid.



An experimental investigation of the reaction showed that it can take place in two directions. If the reaction is carried out under vacuum so that the hydrogen chloride formed is removed immediately from the reaction mixture, the process takes place according to the above-mentioned general system of the phosphazo reaction (I). As in the case of the reaction with phosphorus pentachloride, the reaction is endothermic.

However, if the reaction of phenyl phosphorus tetrachloride with urethan is carried out at atmospheric pressure, it takes place with liberation of heat and alkyl halide, less than one mole of hydrogen chloride being formed. The main reaction product is the diacyl chloride of phenyl phosphinic acid, alkyl halide and difficultly crystallizable substances, similar in nitrogen content to alkyl cyanates. Therefore in the presence of hydrogen chloride the reaction does not stop at the formation of the phosphazo compound, but proceeds further, in accordance with the usual system of thermal decomposition of carbacylphosphazo compounds [3]:



The formation of alkyl halides is probably explained by the hydrohalogenolysis of either the alkyl cyanates or the intermediate reaction products.

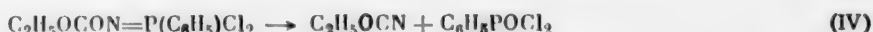
Esters of phenyl dichlorophosphazocarbonic acid are mobile colorless liquids with a pungent odor. As regards their chemical properties, they differ from esters of trichlorophosphazocarbonic acid by their considerably greater basicity.

At room temperature, esters of trichlorophosphazocarbonic acid dissolve hydrogen chloride [7], but this is not accompanied by appreciable liberation of heat. When a solution of hydrogen chloride in esters of trichlorophosphazo-

carbonic acid is heated, the latter decompose almost quantitatively according to the same system [7] as in the absence of hydrogen chloride [1]:



Esters of phenyl dichlorophosphazocarbonic acid absorb hydrogen chloride with liberation of heat. In the presence of hydrogen chloride, esters of phenyl dichlorophosphazocarbonic acid decompose even at 20° in like manner to thermal decomposition of trichlorophosphazocarbacyl compounds.

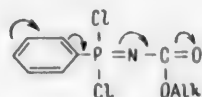


The actual reaction products are the diacyl chloride of phenyl phosphinic acid and the products of further conversions of ethyl cyanate (ethyl chloride, cyanuric acid and ethyl cyanurate).

When esters of phenyl dichlorophosphazocarbonic acid are heated (75-85°) in the absence of hydrogen chloride the reaction takes place mainly in a similar way to (III), i.e., with formation of ethyl chloride and the acyl chloride of isocyanophenyl phosphinic acid.



The increased basicity of the ethyl ester of phenyl dichlorophosphazocarbonic acid is explained by the reaction of π -electrons of the phenyl ring with the conjugated system of the phosphazocarbonyl group, which increases the negative charge of the carbonyl oxygen, i.e., increases its tendency to add a proton.



Evidently, decomposition according to system (IV) precedes the addition of a proton to the molecule of the ethyl ester of phenyl dichlorophosphazocarbonic acid, because decomposition, in the absence of hydrogen chloride, takes place mainly according to system (V); however, at present there are insufficient data for a detailed discussion of the mechanism either the (IV) or (V) type of decomposition.

When the methyl and ethyl esters of phenyl dichlorophosphazocarbonic acid are obtained by system (I), 2 moles of hydrogen chloride are formed. Even when the reaction is carried out in vacuo under conditions which ensure very rapid and complete removal of hydrogen chloride, the latter still reacts to some extent with the esters of phenyl dichlorophosphazocarbonic acid, which leads to splitting of these esters according to system (IV). Therefore the reaction products are 80-90% mixtures of esters of phenyl dichlorophosphazocarbonic acid and 10-20% of the products of their decomposition according to system (IV). When these mixtures are heated to 75-85° they are converted to an 80-90% mixture of the acyl chloride of isocyanophenyl phosphinic acid and the conversion products of ethyl cyanate. Therefore, because the boiling points of the isocyanate and the acyl chloride of phenyl phosphinic acid are very close, the acyl chloride of isocyanophenyl phosphinic acid can only be isolated in the pure form by vacuum distillation with a low yield (~ 25%).

The acyl chloride of isocyanophenyl phosphinic acid is a colorless liquid with an unpleasant, pungent odor, which distills under vacuum without decomposition and is readily soluble in ether and benzene. The acyl chloride is unchanged in the presence of hydrogen chloride; it reacts vigorously with water, alcohols and amines. It is readily hydrolyzed by atmospheric moisture and, therefore, all operations must be carried out in a dry atmosphere.

The reaction mixture obtained by thermal decomposition of the methyl ester of phenyl dichlorophosphazocarbonic acid, containing about 80% of the acyl chloride of isocyanophenyl phosphinic acid, may be used for obtaining certain derivatives of the latter because this reacts with substances containing active hydrogen atoms, for example aromatic amines, far more rapidly than the impurities (including the diacyl chloride of phenyl phosphinic acid). During this process, substances with markedly different physical properties from the impurities are formed, and may therefore readily be isolated in the pure state. Thus, for example, when 80% of the theoretical amount of amine

is added to the "crude" acyl chloride of isocyanophenyl phosphinic acid in ether solution, more than 96% (calculated on the aniline) of completely pure N-phenyl chlorophosphinyl-N'-phenyl urea is precipitated.



But if 90% of aniline is added, the product obtained is contaminated. This proves that the "crude" acyl chloride of isocyanophenyl phosphinic acid contains not less than 80% of the pure substance and that the chlorine atom in N-phenyl chlorophosphinyl-N'-phenyl urea reacts with aromatic amines far more slowly than the isocyanate group.

EXPERIMENTAL

Esters of phenyl dichlorophosphazocarbonic acid. 0.1 g-mole of phenyl phosphorus tetrachloride and 0.1 g-mole of methyl urethan were placed in a round-bottomed flask connected in series with two hydrogen chloride traps and the last trap was immediately connected to a rapidly acting water-jet vacuum pump. The reaction soon commenced, a large amount of hydrogen chloride was liberated, the mixture was cooled and it gradually liquefied. To accelerate the reaction, the flask was placed in a bath heated to 20-30°. The reaction was completed in 20-30 minutes. The yield of hydrogen chloride was 89%, the yield of the crude methyl ester of phenyl dichlorophosphazocarbonic acid was theoretical.

Found %: Cl 28.50, $\text{C}_6\text{H}_5\text{O}_2\text{NPCl}_2$. Calculated %: Cl 28.13.

In spite of the quantitative yield and the satisfactory results of the analysis for chlorine, the reaction product contained a small amount of ether-insoluble impurities; when the substance was treated with anhydrous ether, these were deposited in the form of a flocculent precipitate.

The ethyl ester of phenyl dichlorophosphazocarbonic acid was obtained in a similar way. In this case about 80% of the hydrogen chloride was liberated.

Thermal decomposition of the methyl ester of phenyl dichlorophosphazocarbonic acid. The flask containing the reaction mixture obtained by the reaction of phenyl phosphorus tetrachloride with methyl urethan was connected to a trap (cooled to -80°) and the latter was connected to a water-jet vacuum pump. The contents of the flask were heated rapidly to 70° and the temperature was then raised slowly to 80-85° (~1° per minute) with constant stirring. Very intense liberation of methyl chloride took place at this temperature. When the contents were heated rapidly, decomposition took place with explosive violence. When vigorous liberation of methyl chloride had ceased, the mixture was heated to 100° and it was kept at this temperature for 15-20 minutes. The yield was 100-103%, calculated on the acyl chloride of isocyanophenyl phosphinic acid. For partial removal of the impurities, the reaction mixture was dissolved in 100-120 ml of anhydrous ether and the solution was left overnight. The precipitate which came out was filtered and the solvent was distilled from the filtrate under vacuum. The liquid residue - the "crude" acyl chloride of isocyanophenyl phosphinic acid, containing ~80% of the latter - was contaminated by products of the decomposition of the methyl ester of phenyl dichlorophosphazocarbonic acid according to system (IV). To obtain the pure acyl chloride of isocyanophenyl phosphinic acid, the "crude" product was distilled under vacuum in an efficient column with complete reflux fractionation. The last fraction, which distilled at 110-110.5° (3 mm), was the pure acyl chloride of isocyanophenyl phosphinic acid. The yield was ~25%.

d_4^{20} 1.3761, n_D^{20} 1.5525, M_R 46.82, calc. 46.43.

Found %: Cl 17.92, 17.98; N 6.86, 6.92. $\text{C}_7\text{H}_5\text{O}_2\text{NPCl}$. Calculated %: Cl 17.59; N 6.95.

N-Phenyl chlorophosphinyl-N'-phenyl urea. A) From the pure acyl chloride of isocyanophenyl phosphinic acid. A solution of 0.015 g-mole of aniline in 10 ml of ether was added slowly with cooling by ice water to a solution of 0.015 ml of the acyl chloride of isocyanophenyl phosphinic acid in 10 ml of absolute ether. A colorless crystalline precipitate was formed. After 2 hours the precipitate was filtered at the pump; it was then washed with absolute ether and dried under vacuum over P_2O_5 . The yield was 95%, the m.p. was 129-130°. Crystallization from ethyl acetate or dichloroethane did not increase the melting point.

Found %: Cl 11.47, 11.62; N 9.48, 9.50. Equiv. after hydrolysis 1.97, 1.99; $\text{C}_{13}\text{H}_{12}\text{O}_2\text{N}_2$ PCl .

Calculated %: Cl 12.05, N 9.51. Equiv. 2.00.

B) From the "crude" acyl chloride of isocyanophenyl phosphinic acid. The synthesis was carried out in the same way, but the amount of aniline taken was 20% less than the theoretical. The yield was 96%, calculated on the aniline. The reaction product was in no way different from the compound obtained from the pure acyl chloride of isocyanophenyl phosphinic acid.

Reaction of the ethyl ester of phenyl dichlorophosphazocarbonic acid. 0.1 g-mole of the ethyl ester of phenyl dichlorophosphazocarbonic acid was placed in a three-necked reaction flask equipped with a thermometer, a gas inlet pipe reaching to the bottom and a gas outlet pipe connected to a cold trap (-80°), and a current of dry hydrogen chloride was slowly passed. After 5-7 minutes the temperature of the contents of the reaction flask had risen to $45-50^{\circ}$ (temperature of the surrounding air 20°) and vigorous liberation of gas bubbles throughout the whole reaction mixture commenced. After 30 minutes the reaction mixture was heated to 50° (without stopping the current of hydrogen chloride) and it was kept at this temperature for 2.5 hours. The yield of ethyl chloride was 64%, the b.p. was 12° . The yield of the liquid reaction product was 24.3 g. This product did not contain the acyl chloride of isocyanophenyl phosphinic acid because we did not succeed in obtaining N-phenyl chlorophosphinyl-N'-phenyl urea by the action of aniline. After treatment of the liquid product with excess aniline, 57% of the dianilide of phenyl phosphinic acid was obtained; the m.p. was $209-210^{\circ}$. It was identified by a mixed melt.

Reaction of ethyl urethan with phenylphosphorus tetrachloride at atmospheric pressure. 0.05 g-mole of phenylphosphorus tetrachloride and 0.05 g mole of ethyl urethan were placed in a flask connected to two traps, in series. The trap intended for retaining ethyl chloride was cooled to -80° , the other was filled with a solution of caustic soda to absorb hydrogen chloride. The flask was placed in a bath, heated to 25° . In 20 minutes the reaction mixture had liquefied and its temperature had risen to 35° . After the temperature of the reaction mixture had ceased to rise, the bath was heated to 100° and the reaction mixture was kept at this temperature for 10-15 minutes. By this time, liberation of gas had completely ceased. The yield of ethyl chloride was 84%, the yield of hydrogen chloride was 0.0298 g-mole. The yield of the liquid reaction product was 11.3 g. The product did not contain the acyl chloride of isocyanophenyl phosphinic acid. After treatment with excess aniline, 65% of the dianilide of phenyl phosphinic acid was obtained; the m.p. was $209-210^{\circ}$. It was identified by a mixed melt.

SUMMARY

1. When phenyl phosphorus tetrachloride reacts with urethan, esters of phenyl dichlorophosphazocarbonic acid are formed.
2. When esters of phenyl dichlorophosphazocarbonic acid are subjected to thermal dissociation in the absence of hydrogen chloride they decompose into alkyl halides and the acyl chloride of isocyanophenyl phosphinic acid, whereas in the presence of hydrogen chloride they give the diacyl chloride of phenyl phosphinic acid and alkyl cyanates, which undergo further conversion.
3. When aromatic amines react with the diacyl chloride of isocyanophenyl phosphinic acid, the isocyano group reacts primarily, and N-aryl chlorophosphinyl-N'-phenyl ureas are formed.

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INVESTIGATION OF BIMOLECULAR ALKYLIDENEARYLAMINES

VII. STRUCTURE OF "EIBNER'S BASE"

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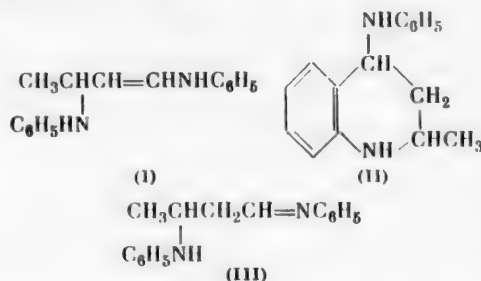
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,

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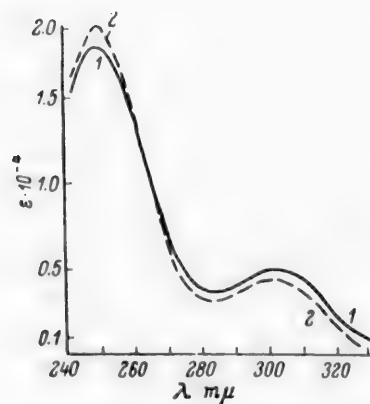
The reaction of aniline with acetaldehyde is known to form two products with the composition $C_{16}H_{18}N_2$, to which Eibner [1] assigned the formulas of stereoisomeric 1,3-dianilino-1-butenes (I).

As one of us showed [2], the first of them, "Eckstein's base" (m.p. 126° "trans-1,3-dianilino-1-butene"), was 2-methyl-4-anilino-1,2,3,4-tetrahydroquinoline (II).



As regards the second isomer of "Eibner's base" (m.p. $85-86^\circ$, "cis-1,3-dianilino-1-butene"), Miller and Plöchl [3] proposed for it the formula of the anil of β -anilino-1,2,3,4-tetrahydroquinoline (III).

As we established, the substance with m.p. $85-86^\circ$ reacts with methylmagnesium iodide to liberate 2 equiv. of hydrogen; consequently, it contains two secondary amino groups, as was considered by Eibner, and therefore, formula (II) is incorrect. However, the substance could not be hydrogenated catalytically in the presence of platinum, indicating that it does not contain an ethylenic bond. Consequently, Eibner's formula (I) is also incorrect.



Ultraviolet absorption spectra of α - and β -isomers. 1) α -isomer; 2) β -isomer.

The third and only possibility is that "Eibner's base" is a tetrahydroquinoline derivative like "Eckstein's base."

These compounds are evidently cis- and trans-isomers with respect to the plane of the hydrogenated ring; however, additional investigations are required to determine the structure of each of them.

Other facts indicate that "Eibner's base" has a tetrahydroquinoline structure.

Thus, 2,6-dimethylaniline, in which both ortho-positions are occupied, does not give a bimolecular product, while 2,4-dimethylaniline, which has one ortho-position free, gives one.

The ultraviolet spectra of "Eckstein's and Eibner's bases" are identical (figure).

"Eibner's base" is very readily converted into quinaldine with the elimination of hydrogen and aniline.

Eibner reported that the substance with m.p. 85-86° may be converted into its stereoisomer with m.p. 126°. He effected this partial conversion by heating the substance above 100° in the presence of iodine or hydrochloric acid. In parallel there was also decomposition to quinaldine, aniline, and hydrogen.

We found that "Eibner's base" may be converted into "Eckstein's base" without a catalyst in better yield by simple boiling in alcohol on a water bath. The reverse conversion did not occur.

Since it is not possible as yet to assign these compounds to the cis- and trans-series, we will subsequently refer to the substance with m.p. 126° as α - and that with m.p. 85-86° as β -2-methyl-4-anilino-1,2,3,4-tetrahydroquinoline.

EXPERIMENTAL

β -2-Methyl-4-anilino-1,2,3,4-tetrahydroquinoline. An 18.60 g sample of distilled aniline was dissolved in a mixture of 300 ml of alcohol and 200 ml of water. To the mixture was added 11.60 ml of acetaldehyde. The reaction mixture was left overnight. The reaction yielded 22.40 g (94%) of a colorless precipitate with m.p. 78°.

The mixture of bases was dissolved in a 10-fold amount of alcohol at 60°. Cooling the solution yielded a colorless crystalline precipitate with m.p. 119° (5.28 g, 23.7%), which, after recrystallization, had m.p. 126° (4.42 g, 19.7%).

The mother solution after isolation of the base with m.p. 126°, was evaporated to 1/4 of its volume and cooled to give a colorless precipitate with m.p. 82° (15.62 g, 70%). The precipitate was recrystallized from ligroin. The colorless acicular crystals had m.p. 85-86° (9.4 g, 42.0%).

Number of active hydrogen atoms found: 1.95, 1.92. $C_{16}H_{18}N_2$.

Conversion of β -isomer into α -isomer. A 10.0 g sample of the base with m.p. 85-86° (β -isomer) was dissolved in 250 ml of alcohol and the solution boiled on a water bath for 5 hr. After distillation of more than 2/3 of the alcohol, the mixture was cooled. There precipitated colorless crystals with m.p. 122°, which, after recrystallization from alcohol, had m.p. 126° and did not depress the melting point of the α -isomer obtained above. The weight of the precipitate was 0.92 g.

The alcohol remaining in the mother solution was removed completely and after solution in ligroin, the residue gave a further 0.70 g of the α -isomer.

Decomposition of the β -isomer by the action of acetic anhydride. To 11.9 g of the β -isomer of the base was added 32 ml of acetic anhydride. The mixture was left for about an hour until the starting material dissolved completely and then the unreacted acetic anhydride was removed by distillation. The residue was vacuum distilled. Two fractions were obtained at 12 mm: the 1st had b.p. 85-90° and reacted with picric acid to give quinaldine picrate with m.p. 193°, which did not depress the melting point of an authentic sample.

The 2nd fraction, which solidified rapidly, had b.p. 90-130° and was recrystallized from toluene. The colorless scaly crystals had m.p. 114° after a second purification and did not depress the melting point of acetanilide.

Reaction of 2,6-dimethylaniline with acetaldehyde. A 5.1 g sample of 2,6-dimethylaniline was mixed with 2.3 ml of acetaldehyde. The liquid evolved heat strongly and became milk white. After it had stood for a short time, water (0.8 g) separated.

The oil was dissolved in ether and dried over sodium sulfate.

After removal of the ether, the liquid was heated on an oil bath. The starting arylamine distilled at 210-211°. The residue in the flask was treated with 40 ml of 20% sulfuric acid. The brown solution had the odor of crotonaldehyde. The mixture was steam distilled. The crotonaldehyde was extracted from the distillate with ether, dried over calcium chloride, the ether removed, and the product distilled at 100-105°. The weight was 0.45 g and the p-nitrophenylhydrazone had m.p. 184-185°.

The residue in the flask after steam distillation was made alkaline and steam distilled again. Extraction, drying, removal of the ether, and distillation of the oil yielded 1.85 g of 2,6-dimethylaniline.

SUMMARY

"Eibner's base" is one of the stereoisomers of 2-methyl-4-anilino-1,2,3,4-tetrahydroquinoline.

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HYDROGEN BOND AND SOLVATOCHROMISM OF SOME CYANINE DYES

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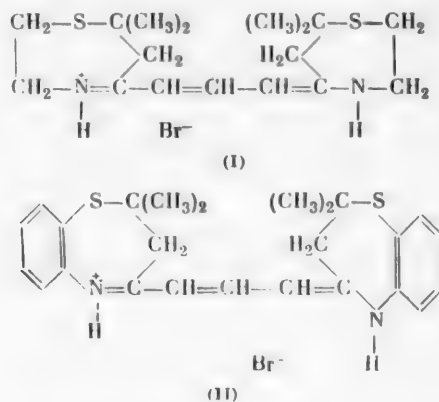
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The phenomenon of solvatochromism, i.e., a change in the color of a dye with a change from one neutral solvent to another, is known to be characteristic of so-called intramolecular dyes, whose molecules may be represented both in a nonpolar form and in the form of a bipolar ion. The solvatochromism of these dyes is explained by the different degree of polarization of their molecules, depending on the polarizing power of the solvent [1-3]. The color of saltlike dyes, basic or acidic, normally depends little on the solvent.

However, we observed peculiar solvatochromism in a new group of saltlike polymethyne dyes, which are derivatives of tetrahydroheptathiazine, dihydrobenzoheptathiazine, and dihydrobenzoheptadiazine, containing hydrogen atoms and not hydrocarbon radicals at the nitrogen atoms [4-6].

These dyes have one absorption maximum in some solvents and a different maximum in other organic solvents with the value of these maxima practically independent of the dielectric constants of the solvents. As an example, in Table 1 we give the absorption maxima of two dyes we synthesized, (I) and (II).



The data in Table 1 show that the absorption maxima of the dyes (I) and (II) in the solvents 1-9 are almost the same [with the exception of dye (I) in ethyl oxalate], despite the difference in their polarities and chemical natures.

A common characteristic of all these solvents is their power to form hydrogen bonds with the solute. On the other hand, in solvents 12-14, which are incapable of forming hydrogen bonds, the maxima of the same dyes lie approximately 50 mμ further into the long-wave region of the spectrum.

Ethyl oxalate, tetrahydrofuran, and dioxane are exceptions to this rule. Two absorption maxima are observed for dye (I) in these solvents. The short-wave maximum corresponds to the solvated state, like that which was observed in the other oxygen-containing solvents. However, its wavelength was slightly displaced into the long-wave region.

A similar displacement of the absorption maximum was also observed for the dye (II) in tetrahydrofuran and in dioxane. The long-wave absorption maximum for dye (I) corresponded to the unsolvated molecule.

TABLE 1

Exp. no.	Solvent	Dye (I)		Dye (II)	
		λ_{\max} (in m μ)	$\epsilon \cdot 10^{-4}$	λ_{\max} (in m μ)	$\epsilon \cdot 10^{-4}$
1	Water	440	10.25	—	—
2	Methanol	448	8.68	499	10.72
3	Acetic acid	440	4.02	495	8.35
4	Acetone	446	8.68	498	8.40
5	Formamide	445	8.50	499	6.70
6	Nitromethane	443	5.69	494	3.50
7	β, β' -Dichloroethyl ether	445	4.75	500	2.67
8	Acetone	442	10.62	500	1.67
9	Ethyl oxalate	465, 490	2.22, 1.42	500	6.62
10	Tetrahydrofuran	473, 498	1.74, 1.87	517	2.55
11	Dioxane	473, 498	—	535	2.67
12	Chloroform	500	6.12	550	4.37
13	Chlorobenzene	500	5.87	553	2.42
14	Benzene	499	3.37	554	1.34

Figure 1 gives absorption curves for dye (I) in some solvents. As the figure shows, the same dye behaves in different solvents as two individual substances with different maxima and forms of absorption curve. The form of the curve in acetone differs somewhat. In addition to the main absorption maximum, two inflections in the region of 465 and 495 m μ are observed in this case. An analogous picture is obtained in methyl ethyl ketone. An analogous picture is also observed for dye (II) (Fig. 2). The absorption maxima in solvents forming a complex with the dye through a hydrogen bond lie approximately 50 m μ closer to the short-wave region in comparison with the absorption maxima of dye (II) in solvents which do not form a hydrogen bond. In tetrahydrofuran, the absorption maximum of the dye (II)–solvent complex is displaced toward shorter wavelengths by 33 m μ (curve 4).

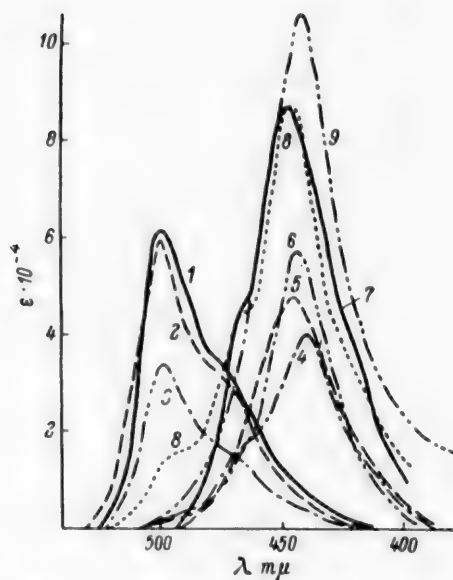


Fig. 1. Absorption spectra of solutions of carbocyanine (I). 1) In chloroform; 2) in chlorobenzene; 3) in benzene; 4) in acetic acid; 5) in β, β' -dichloroethyl ether; 6) in nitromethane; 7) in methanol; 8) in acetone; 9) in acetonitrile.

alcohol concentration of 20%, the absorption maximum characteristic of a chloroform solution disappeared and there remained only an inflection on the curve in this region. The presence of an isosbestic point for all absorption curves (apart from the curve for pure methanol) indicates that in chloroform and in alcohol the dye is present in two definite individual forms: one is the dye unassociated with solvent and the other is the dye associated with a definite number of alcohol molecules (apparently two alcohol molecules as the two NH groups, which are capable of forming

The heights of the absorption maxima (values of $\epsilon \cdot 10^{-4}$) for dyes (I) and (II) in acetic acid and acetonitrile are noteworthy. Dye (I) has a value of 4.02 for $\epsilon \cdot 10^{-4}$ at the absorption maximum in acetic acid and 10.62 in acetonitrile. On the other hand, dye (II) has 8.35 for $\epsilon \cdot 10^{-4}$ in acetic acid and 1.67 in acetonitrile. These interesting facts have not been explained satisfactorily as yet.

We obtained interesting data on studying the absorption curves of dye (I) in a mixture of methanol and chloroform. As Fig. 3 shows, the addition of 5% of alcohol to a chloroform solution of the dye first produced an inflection on the absorption curve (curve 2) and with an increase in the alcohol concentration, there appeared a second maximum in the region of 448 m μ and there was a change in the absorption intensity: it decreased in the long-wave region and increased in the region where an alcohol solution shows intense absorption. With an

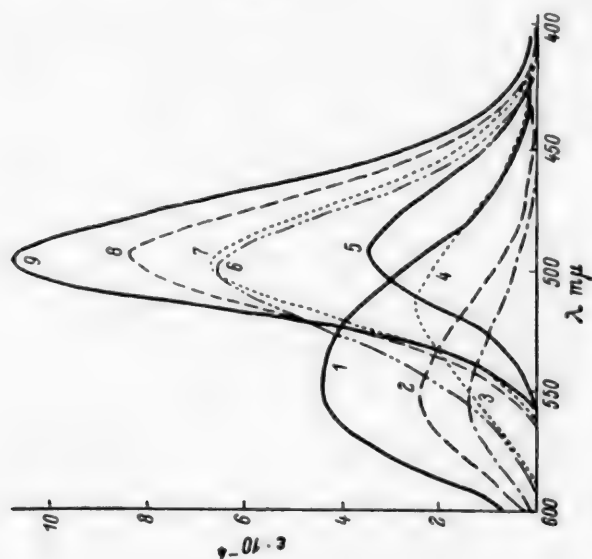


Fig. 2. Absorption spectra of solutions of the carboyanine (II). 1) In chloroform; 2) in benzene; 3) in benzene; 4) in tetrahydrofuran; 5) in nitromethane; 6) in ethyl oxalate; 7) in formamide; 8) in acetic acid; 9) in methanol.

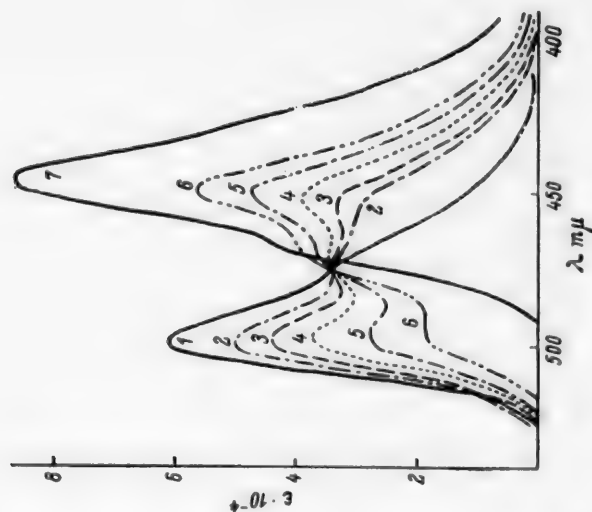


Fig. 3. Absorption spectra of solutions of the carboyanine (I) in mixtures of methanol and chloroform (by volume). 1) In 100% chloroform; 2) in 5% methanol; 3) in 10% methanol; 4) in 15% methanol; 5) in 20% methanol; 6) in 7% methanol; 7) in 100% methanol.

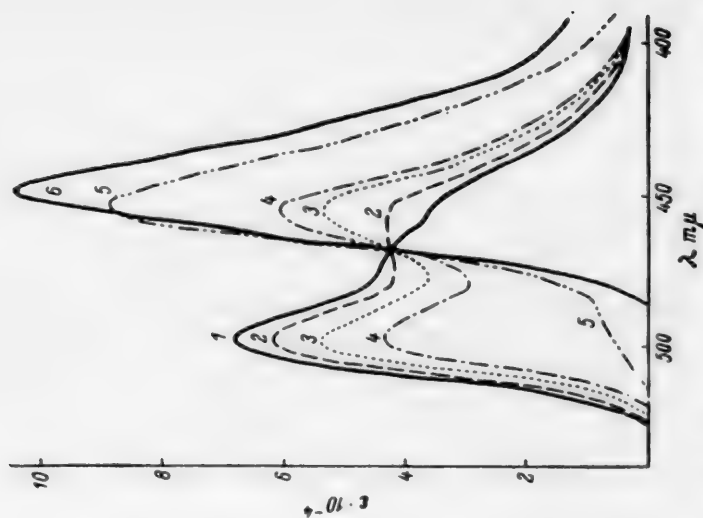
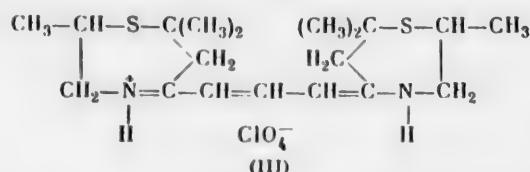


Fig. 4. Absorption spectra of solutions of the carboyanine (III) in mixtures of methanol and chloroform (by volume). 1) In 100% chloroform; 2) in 0.4% methanol; 3) in 1% methanol; 4) in 5% methanol; 5) in 20% methanol; 6) in 100% methanol.

hydrogen bonds, are equivalent). The dye (III), which is the closest homolog of the dye (I), was found to be more sensitive to a change of the concentration of alcohol in chloroform.



In this case the presence of even 0.4% of alcohol in a chloroform solution of the dye produced an appreciable inflection on the absorption curve (Fig. 4). In a 1% solution of alcohol in chloroform there appeared two absorption maxima of approximately the same intensities and at the same wavelengths as those observed for solutions of the dye (III) in pure alcohol and in pure chloroform (curve 3). With an increase in the concentration of alcohol in chloroform, the intensity of the long-wave maximum decreased and even at 20% alcohol, only an inflection remained (curve 5). The presence of a clear isosbestic point in this case demonstrates the existence of an equilibrium of two definite individual forms of the dye in the solutions investigated.

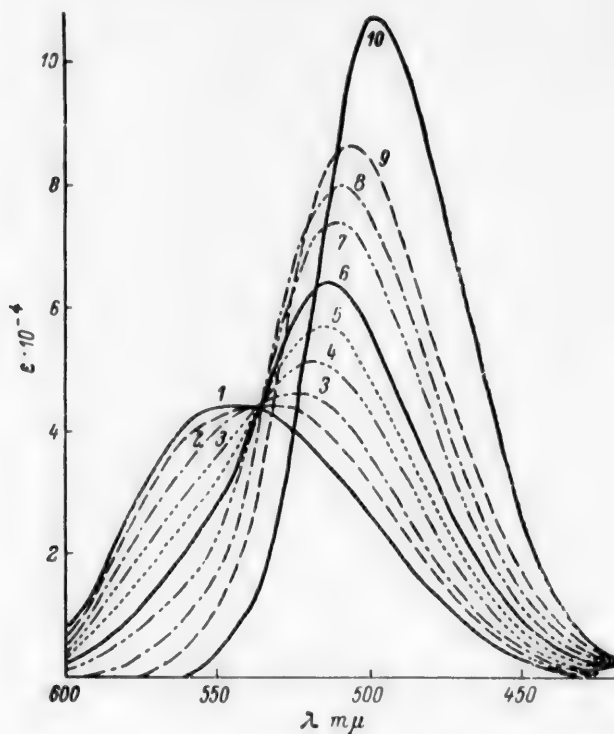
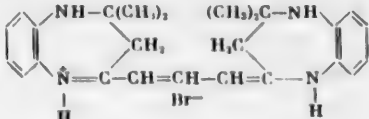
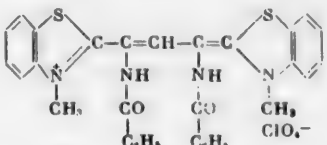
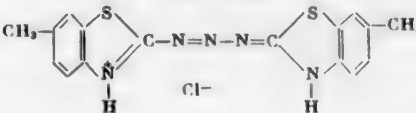


Fig. 5. Absorption spectra of solutions of the carbocyanine (II) in mixtures of methanol and chloroform (by volume). 1) In 100% chloroform; 2) 0.5% methanol; 3) in 1% methanol; 4) in 2% methanol; 5) in 3% methanol; 6) in 5% methanol; 7) in 10% methanol; 8) in 20% methanol; 9) in 40% methanol; 10) in 100% methanol.

We obtained analogous absorption curves on measuring the spectra of the dye (I) in a mixture of chloroform + acetic acid. The color of a chloroform solution of the dye was found to be less sensitive to acetic acid. An inflection appeared on the absorption curve at 10% of acetic acid in chloroform, while the second maximum, which is characteristic of a solution in acetic acid, was formed only in a solution containing 60% of the acid in chloroform.

TABLE 2

Sub- stance no.	Dye	Liter- ature	λ_{\max} (in m μ)		Difference (in m μ)
			alco- hol	chlor- oform	
(IV)		[6]	515	565	50
(V)		[7]	550	575	25
(VI)		[8]	480	495	15

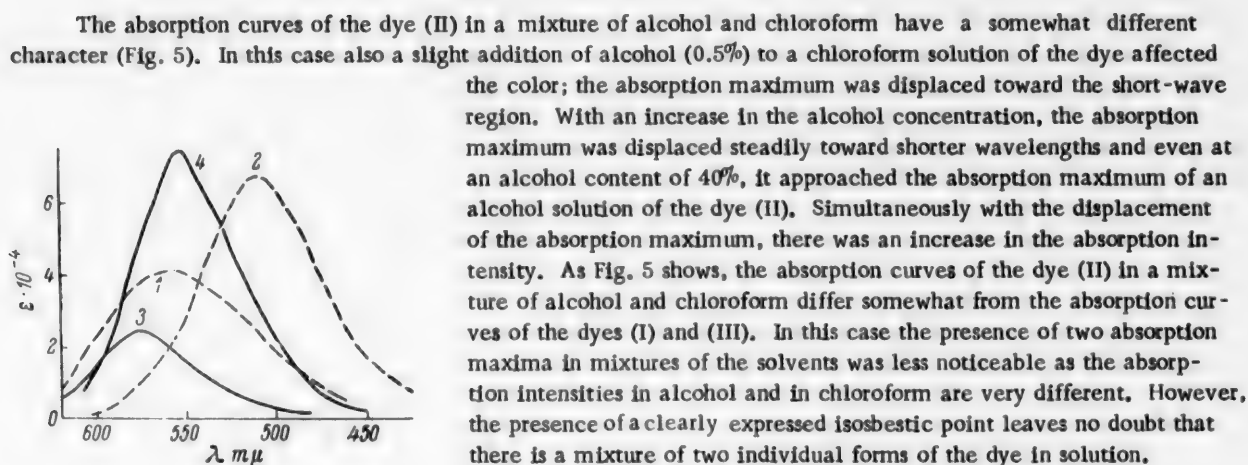


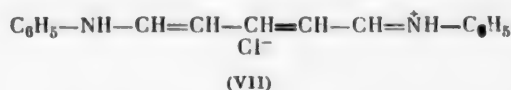
Fig. 6. Absorption of spectra of solutions of the carbocyanines (IV) and (V). 1) Dye (IV) in chloroform; 2) dye (IV) in alcohol; 3) dye (V) in chloroform; 4) dye (V) in alcohol.

It seemed interesting to look for the form of solvatochromism described with other saltlike dyes containing an NH group in the molecule. For this purpose we measured the absorption curves of two more cyanine dyes (IV) and (V), which have been described in the literature (Table 2).

As the data in Table 2 and also the nature of the absorption curves (Fig. 6) of the dyes (IV) and (V) show, here also there is undoubtedly the formation of hydrogen bonds with alcohol molecules.

The difference in the positions of the absorption maxima of the azacyanine (VI) in alcohol and chloroform of 15 m μ evidently also indicates the presence of a hydrogen bond between dye and alcohol molecules [5].

However, the absorption maxima of salts of glutaric aldehyde anilides such as (VII), which also contain hydrogen atoms at the nitrogen, in alcohol and chloroform were identical.



The importance of hydrogen bonds in solvatochromism has been pointed out repeatedly. Thus, for example, in a study of the absorption spectra of some merocyanines, Bayliss and McRae [9] came to the conclusion that they depend more on the capacity of the solvent to form hydrogen bonds than on its dielectric constant. The same was reported by Kumler [10] for p-nitroaniline. However, most authors [10-12] agree that hydrogen bonds play a substantial, but not the main role in solvatochromism.

From our work it follows that the main reason for the change in the color of saltlike cyanine dyes containing hydrogen atoms and not hydrocarbon radicals at the nitrogen atoms of the heterocycles is the formation of hydrogen bonds with the solvent through the NH groups.

EXPERIMENTAL

Bis(2,7,7-trimethyltetrahydrohepta-1,4-thiazine-5)-trimethynecyanine perchlorate (III). A mixture of 2.71 g of 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine perchlorate, 1.48 g of orthoformic ester, and 10 ml of pyridine was heated on a water bath for 30 min (until the mixture dissolved completely). Washing with ether liberated an oil, which solidified with further washing. After recrystallization from alcohol, the carbocyanine (yellow crystals) had decomp. p. 205°. The yield was 0.41 g (18%).

Found %: N 6.25, 5.98; Cl 7.61, 7.76. $C_{19}H_{33}O_4N_2S_2Cl$. Calculated %: N 6.18; Cl 7.82.

Bis(2,2-dimethyldihydrobenzohepta-1,5-thiazine-4)-trimethynecyanine bromide (II). A mixture of 2.86 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrobromide, 1.48 g of orthoformic ester, 15 ml of acetic anhydride, and 5 drops of pyridine was heated on a water bath until the mixture dissolved completely (30 min). On heating, the mixture acquired a red color. On cooling, the solution deposited red crystals of the carbocyanine. The crystals were collected and washed with water, alcohol, and ether. After recrystallization from alcohol, the dye had m.p. 215°. The yield was 1.1 g (48%).

Found %: N 5.56, 5.64; Br 15.66, 15.82. $C_{25}H_{29}N_2S_2Br$. Calculated %: N 5.59; Br 15.93.

Solutions of the dye (II) at low concentrations in most solvents lost the elements of the acid. A certain amount of dry hydrogen chloride was added to the solution to prevent this phenomenon.

The absorption spectra of dyes given in Figs. 1 and 2 were measured with solutions with the concentration of $1 \cdot 10^{-5}$ M on an SF-4 spectrophotometer. The absorption spectra of dyes given in Figs. 3-6 were measured with solutions with a concentration of $2 \cdot 10^{-5}$ M on SF-2M and SF-4 spectrophotometers.

SUMMARY

1. It was established that some saltlike cyanine dyes show solvatochromism, which is associated with the formation of a dye-solvent complex through a hydrogen bond.

2. It was observed that with the formation of a solvent-dye complex, the absorption maximum is displaced into the short-wave region by approximately 50 mμ for saltlike polymethyne dyes which are derivatives of tetrahydroheptathiazine, dihydrobenzoheptathiazine, and dihydrobenzoheptadiazine, containing hydrogen atoms and not hydrocarbon radicals at the nitrogen atoms.

3. In mixtures of alcohol with chloroform, these dyes form a series of curves with an isobestic point, whence it follows that the complex with alcohol has a simple and constant composition, probably 2 moles of alcohol to 1 mole of dye.

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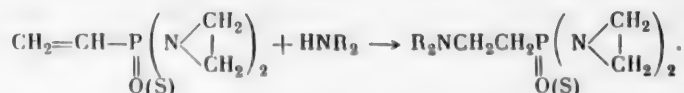
DIETHYLENIMIDES OF β -AMINOETHYLPHOSPHINIC AND THIOPHOSPHINIC ACIDS. II

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The chemical properties of diethylenimidovinylphosphonates and vinylthiophosphonates have hardly been studied [1]. However, we showed previously that these substances, like esters of vinylphosphinic acid, add mercaptans and alcohols to form the corresponding ethylenimides of alkylphosphinic and alkylthiophosphinic acids, containing ether and thioether groups in the radical bound to the phosphorus through carbon [2]. Continuing these investigations, we studied the addition of secondary and primary amines to diethylenimides of vinylphosphinic and vinylthiophosphinic acids. The amines we used were diethylamine, ethylenimine, piperidine, morpholine, dibenzylamine, and allylamine. These amines add to amides of vinylphosphinic and vinylthiophosphinic acids to form imides of β -aminoethylphosphonates and thiophosphonates (Table 1).



The order of addition of amines to diethylenimides of vinylphosphinic and vinylthiophosphinic acids is as shown above since the orientation of addition is determined by the polar state of the multiple bond.

The reaction proceeded particularly readily in the case of diethylamine, piperidine, and ethylenimine. These amines added at room temperature in 1.5-2 days and at 40-50° in 4-5 hr. Dibenzylamine and allylamine added in the presence of catalytic amounts of sodium alcoholate. In all cases the reaction proceeded best without a solvent with an equimolecular amount or a small excess of the amine. It should also be noted that the addition of amines to imides of vinylphosphinic and vinylthiophosphinic acids was much more difficult than the addition of amines to neutral esters of vinylphosphinic acid [3]. This is explained by the different polarity of the multiple bond in imides and esters of vinylphosphinic acid.

The addition products of piperidine, morpholine, and diethylamine to imides of vinylphosphonates and vinylthiophosphonates were purified by vacuum distillation (10^{-4} mm); the other imides of β -aminoethylphosphonates decomposed on distillation. The latter substances were analyzed after being kept in vacuum (0.1 mm) for 2 hr. The analysis data indicate that these substances were obtained in a comparatively pure form without distillation. For additional characterization, the undistilled β -aminoethylphosphonates were converted into picrates (Table 2).

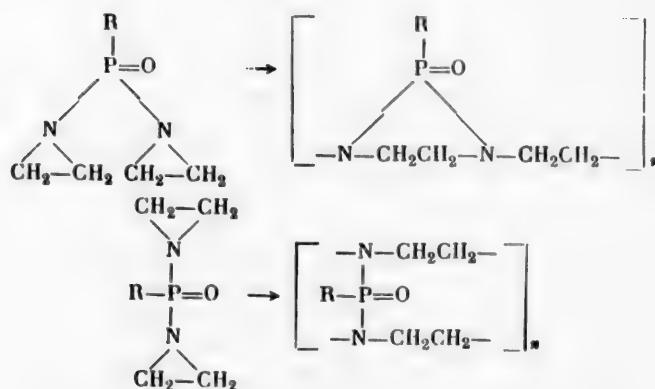
All the diethylenimides of aminothiophosphonates and aminophosphonates were colorless viscous liquids, which were soluble in benzene, chloroform, ether, and alcohol; the former (in contrast to the latter) were insoluble in water. The substances were stable at temperatures below 0°, but prolonged storage at room temperature led to gradual polymerization (to a vitreous state). Thus, the diethylenimide of β -diethylaminoethylphosphinic acid was converted into a slightly yellowish vitreous polymer when stored for 1.5 months.

It must be assumed that the polymerization of the ethylenimides into macromolecular compounds occurs as a result of opening of the ethylenimide rings. Linear polymers without a phosphorus residue in the chain and with a phosphorus residue binding the main chains of the macromolecule are evidently obtained.

The possibility of the formation of three-dimensional polymers cannot be excluded. The polymerization products were not investigated in more detail.

TABLE 1

Sample no.	Formula of substance	Empirical formula	Name of substance
1	$\begin{array}{c} \text{C}_6\text{H}_5 \\ \text{C}_6\text{H}_5 \end{array} \text{N}-\text{CH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{22}\text{N}_3\text{SP}$	Diethylenimide of β -diethylaminoethylthiophosphonic acid
2	$\begin{array}{c} \text{C}_6\text{H}_5 \\ \text{C}_6\text{H}_5 \end{array} \text{N}-\text{CH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{O} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{22}\text{ON}_3\text{P}$	Diethylenimide of β -diethylaminoethylphosphonic acid
3	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \text{N}-\text{CH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_8\text{H}_{16}\text{N}_3\text{SP}$	Diethylenimide of β -ethyleniminoethylthiophosphonic acid
4	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \text{N}-\text{CH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{O} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_8\text{H}_{16}\text{ON}_3\text{P}$	Diethylenimide of β -ethyleniminoethylphosphonic acid
5	$\text{CH}_2=\text{CHCH}_2\text{NHCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{18}\text{N}_3\text{SP}$	Diethylenimide of β -allylaminoethylthiophosphonic acid
6	$\text{CH}_2=\text{CHCH}_2\text{NHCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{O} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{18}\text{ON}_3\text{P}$	Diethylenimide of β -allylaminoethylphosphonic acid
7	$\begin{array}{c} \text{C}_6\text{H}_5\text{CH}_2 \\ \text{C}_6\text{H}_5\text{CH}_2 \end{array} \text{N}-\text{CH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{20}\text{H}_{26}\text{N}_3\text{SP}$	Diethylenimide of β -dibenzylaminoethylthiophosphonic acid
8	$(\text{C}_6\text{H}_5\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{O} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{20}\text{H}_{26}\text{ON}_3\text{P}$	Diethylenimide of β -dibenzylaminoethylphosphonic acid
9	$\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \quad \\ \text{CH}_2-\text{CH}_2 \end{array} \text{NCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{11}\text{H}_{22}\text{N}_3\text{SP}$	Diethylenimide of β -piperidylethylthiophosphonic acid
10	$\begin{array}{c} \text{O}-\text{CH}_2-\text{CH}_2 \\ \quad \\ \text{O}-\text{CH}_2-\text{CH}_2 \end{array} \text{NCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{S} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{20}\text{ON}_3\text{SP}$	Diethylenimide of β -morpholyethylthiophosphonic acid
11	$\begin{array}{c} \text{O}-\text{CH}_2-\text{CH}_2 \\ \quad \\ \text{O}-\text{CH}_2-\text{CH}_2 \end{array} \text{NCH}_2\text{CH}_2\text{P} \begin{array}{c} \parallel \\ \text{O} \end{array} \left(\text{N} \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 \end{array} \right)_2$	$\text{C}_{10}\text{H}_{20}\text{O}_2\text{N}_3\text{P}$	Diethylenimide of β -morpholyethylphosphonic acid



EXPERIMENTAL

***N,N'*-Diethylenimide of *N'*-piperidino- β -ethylthiophosphonic acid (typical preparation).** To 9.5 g of the diethylenimide of vinylthiophosphonic acid was added 5.1 g of piperidine and the reaction mixture stirred at room temperature for 5-6 hr and left overnight or heated at 40-50° with stirring for 4-5 hr. The substance was isolated by

Bath temperature (at 10^{-4} mm)	d_4^{20}	n_D^{20}	Found %			Calculated %			Yield, %
			P	S	N	P	S	N	
95—100°	1.1081	1.5392	12.45, 12.31	12.85, 12.80	16.51, 16.31	12.55	12.95	17.0	61.5
107—110	1.0821	1.4996	13.8, 13.9	—	18.23, 18.00	13.4	—	18.15	40
Not dissolved	1.1264	1.5590	14.20, 14.10	14.76, 14.61	19.06, 19.11	14.28	14.72	19.33	Quantitative
Not dissolved	1.1596	1.5153	—	—	20.67, 20.54	—	—	20.84	Quantitative
Not dissolved	1.1223	1.5520	13.65, 13.59	14.07, 14.03	18.20, 18.06	13.4	13.85	18.15	Quantitative
Not dissolved	1.1141	1.5170	—	—	17.84, 17.64	—	—	19.5	Quantitative
Not dissolved	1.1123	1.5860	8.33, 8.27	8.84, 8.64	11.4, 11.4	8.35	8.63	11.3	Quantitative
Not dissolved	1.0798	1.5508	8.25, 8.10	—	11.26, 10.97	8.74	—	11.82	Quantitative
100	1.1258	1.5545	—	—	16.0, 16.31	—	—	16.2	64.0
110—115	1.1392	1.5531	—	—	15.93, 16.13	—	—	16.05	43.4
120	1.1399	1.5112	—	—	17.06	—	—	17.1	35.4

vacuum distillation (10^{-4} mm) at a bath temperature of 100–110°. The yield was 9.85 g (67.5%). The substance was a colorless viscous liquid, which dissolved readily in benzene, acetone, and alcohol, and sparingly in water. The properties of the compound obtained are given in Table 1. Compounds 2–7 (Table 1) were prepared analogously. The substances which were not distilled were kept in vacuum (0.1 mm) at 40–50° before analysis. The yields of the undistilled products, which were comparatively pure, reached 100%.

N,N' -Diethylenimide of N' -dibenzylamino- β -ethylthiophosphinic acid (typical preparation). A mixture of 4.35 g of the diethylenimide of vinylthiophosphinic acid, 4.93 g of dibenzylamine, and catalytic amounts of sodium ethylate was stirred at 80° for 12 hr to give a quantitative yield of a yellow oily substance, which was soluble in benzene, alcohol, and chloroform, and sparingly soluble in water and ether, and could not be distilled in vacuum (10^{-4} mm). Compounds 8–10 (Table 1) were prepared analogously.

Picrates of diethylenimidoaminophosphonates. To an ether or benzene solution of the appropriate aminophosphonate was slowly added a solution of picric acid in benzene with cooling. The precipitated crystals or oil (which crystallized on trituration with ether) were collected, washed carefully with dry ether, and dried. The picrates of the diethylenimides of β -piperidinoethylthiophosphonate and β -dibenzylaminoethylthiophosphonate were recrystallized from mixtures of benzene and ligroin, and benzene and alcohol, respectively.

SUMMARY

It was shown that primary and secondary amines add to diethylenimides of vinylphosphinic and vinylthiophosphinic acids to form previously unknown diethylenimides of β -aminoethylphosphinic and thiophosphinic acids.

TABLE 2

Sam- ple no.	Formula of substance	Empirical formula	Name of substance	M.p.	% N	
					found	calculated
1.	$ \begin{array}{c} \text{C}_4\text{H}_5(\text{NO}_2)_3\text{OH} \\ \\ \text{H}_3\text{C}-\text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \\ \\ \text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \end{array} $	$\text{C}_{17}\text{H}_{25}\text{O}_7\text{N}_6\text{SP}$	Diethylenimide of β -piperidylthiophosphinic acid. Picrate.	112–113°	17.14	17.2
2	$ \begin{array}{c} \text{C}_4\text{H}_5(\text{NO}_2)_3\text{OH} \\ \\ (\text{C}_4\text{H}_5\text{CH}_2)_2\text{NCH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \\ \\ \text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \end{array} $	$\text{C}_{26}\text{H}_{29}\text{O}_7\text{N}_6\text{SP}$	Diethylenimide of β -dibenzylaminoethylthiophosphinic acid. Picrate.	120–122	14.12, 14.01	13.98
3	$ \begin{array}{c} \text{C}_4\text{H}_5(\text{NO}_2)_3\text{OH} \\ \\ \text{CH}_2=\text{CH}-\text{CH}_2-\text{NH}-\text{CH}_2\text{CH}_2-\text{P}(=\text{O})(\text{CH}_3)_2 \\ \\ \text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{O})(\text{CH}_3)_2 \end{array} $	$\text{C}_{15}\text{H}_{21}\text{O}_8\text{N}_6\text{P}$	Diethylenimide of β -allylaminoethylphosphonic acid. Picrate	69–70	18.84, 18.73	18.91
4	$ \begin{array}{c} \text{C}_4\text{H}_5(\text{NO}_2)_3\text{OH} \\ \\ (\text{C}_4\text{H}_5\text{CH}_2)_2\text{NCH}_2\text{CH}_2-\text{P}(=\text{O})(\text{CH}_3)_2 \\ \\ \text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{O})(\text{CH}_3)_2 \end{array} $	$\text{C}_{26}\text{H}_{29}\text{O}_8\text{N}_6\text{P}$	Diethylenimide of β -dibenzylaminoethylphosphinic acid. Picrate.	103–104	14.48, 14.42	14.38
5	$ \begin{array}{c} \text{C}_4\text{H}_5(\text{NO}_2)_3\text{OH} \\ \\ \text{CH}_2=\text{CHCH}_2\text{NHCH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \\ \\ \text{CH}_2\text{CH}_2-\text{N}-\text{CH}_2\text{CH}_2-\text{P}(=\text{S})(\text{CH}_3)_2 \end{array} $	$\text{C}_{15}\text{H}_{21}\text{O}_7\text{N}_6\text{SP}$	Diethylenimide of β -allylaminoethylthiophosphinic acid. Picrate.	116–117	18.02, 18.13	18.22

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

DIETHYLENIMIDES OF ALKYL- AND ALKENYLTHIO-
PHOSPHINIC AND PHOSPHINIC ACIDS AND SOME
OF THEIR PROPERTIES: I

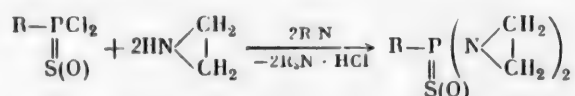
K. A. Petrov, A. I. Gavrilova, V. K. Shatunov,
and V. P. Korotkova

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In contrast to phosphates, ethylenimidophosphonates have been studied very little. There are several papers [1] on the preparation of these compounds; our previous paper was devoted to the synthesis and study of the properties of diethylenimidophosphonates and diphosphonates [2]. Ethylenimidothiophosphates have not been studied at all, while thionophosphates, which are of similar structure, are of the greatest practical interest of all the derivatives of phosphorus acids synthesized containing ethylenimide residues.

In the present work we describe diethylenimides of alkyl- and alkenylthiophosphinic and allylphosphinic acids. We studied the addition of mercaptans and alcohols to diethylenimides of vinylphosphinic and vinylthiophosphinic acids in order to prepare imidophosphonates and thiophosphonates containing ether and thioether groups in the radical to the phosphorus directly through carbon.

The diethylenimides of alkyl- and alkenylthiophosphinic and allylphosphinic acids were obtained by the reaction of the appropriate acid chlorides with ethylenimine in anhydrous benzene or ether in the presence of a tertiary base (as a hydrogen chloride acceptor) at 5-10° according to the scheme:



The substances obtained were colorless liquids, which dissolved readily in water and organic solvents. Some of them crystallized on long standing. Almost all the substances were purified by distillation. However, they could only be distilled in high vacuum as they polymerized instantaneously at 120° and above and a pressure of 0.1 mm. We were unable to distill only the diethylenimide of β -chloroethylthiophosphinic acid, which polymerized explosively at 100-102° even at a pressure of 10^{-4} mm. This is evidently explained by the fact that the chlorine in the diethylenimide of β -chloroethylthiophosphinic acid is readily eliminated by heating in the form of hydrogen chloride, which produces opening of the ethylenimine rings and spontaneous polymerization. The properties and yields of the substances obtained are given in Table 1.

The diethylenimides of vinylphosphinic and thiophosphinic acids, like the esters [3] add mercaptans and alcohols.

The reaction with mercaptans proceeded at 60° and was complete in 14-15 hr. The reaction was accelerated in the presence of catalytic amounts of sodium alcoholate. Ethyl mercaptan added more readily than butyl mercaptan. The reaction proceeded according to the scheme:



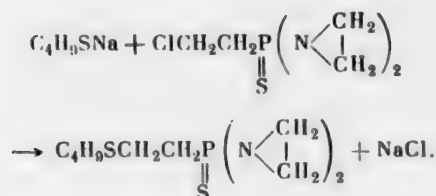
The yields of the addition products reached 50-60%.

TABLE 1

Formula	Empirical formula	B.p. (pressure in mm)	d ₄ ²⁰	n _D ²⁰	M.P.		Calculated %				Found %				Yield, %
					calc.	found	P	S	N	Cl	P	S	N	Cl	
$\text{ClCH}_2\text{P}(\text{N}(\text{CH}_2)_2)_2$	$\text{C}_5\text{H}_{10}\text{SN}_2\text{P}_2\text{Cl}$	84° (0.15)	1.5048	1.5565	49.26	49.49	15.75	16.3	14.22	18.0	15.76, 16.04	16.42, 16.4	14.34, 14.06	17.92, 17.85	59.0
$\text{CH}_2\text{P}(\text{N}(\text{CH}_2)_2)_2$	$\text{C}_3\text{H}_{11}\text{SN}_2\text{P}$	72-73 (1.0)	1.1467	1.5475	44.42	44.83	19.13	19.74	17.25	—	19.26, 19.48	20.06, 20.44	17.02, 17.14	—	78.0
$\text{ClCH}_2\text{CH}_2\text{P}(\text{N}(\text{CH}_2)_2)_2$	$\text{C}_6\text{H}_{12}\text{SN}_2\text{P}_2\text{Cl}$	Not distilled	1.2390	1.5538	53.90	54.53	14.82	15.18	13.3	16.85	14.66, 14.58	15.12, 14.96	13.07, 13.23	16.58, 16.16	Quantitative
$\text{CH}_2=\text{CHP}(\text{N}(\text{CH}_2)_2)_2$	$\text{C}_6\text{H}_{11}\text{SN}_2\text{P}$	72-74 (0.4)	1.1476	1.5558	48.61	48.77	17.75	18.4	16.05	—	17.74, 17.11	18.51, 18.78	15.86, 15.92	—	76.0
$\text{CH}_2=\text{CHCH}_2\text{P}(\text{N}(\text{CH}_2)_2)_2$	$\text{C}_7\text{H}_{13}\text{ON}_2\text{P}$	70-80 (10-4)*	1.1300	1.5082	45.2	45.12	18.0	—	16.2	—	18.17, 18.32	—	15.94, 15.86	—	68.5

* Bath temperature.

The structure of the products obtained was confirmed by the reaction of the diethylenimide of β -chloroethylthiophosphinic acid with sodium butyl mercaptide.



The reaction proceeded under mild conditions and gave a better yield than the addition of butyl mercaptan to the diethylenimide of vinylthiophosphinic acid.

The constants of S-butyl-S-dimethylenedithylenimidothiophosphonate were the same for samples obtained by the two methods. The substance was an immobile liquid, which was stable during storage and distilled only in high vacuum. Its properties are given in Table 2.

Alcohols in contrast to mercaptans, added with more difficulty to the diethylenimides of vinylphosphinic and thiophosphinic acids. The products from addition of ethanol and butanol could be obtained in low yields only by prolonged heating of the reaction mixture in the presence of alcoholates. However, it was difficult to isolate the substances obtained in this way in a pure form because of the similarity of the boiling points of the starting diimide of the vinylphosphonate and the final addition product. Substances of suitable purity were obtained in satisfactory yields by the action of alcoholates on diethylenimides of β -chloroethylphosphinic acid. The properties of the substances obtained are given in Table 2.

EXPERIMENTAL

N,N'-Diethylenimide of chloromethylthiophosphinic acid (typical preparation). To 11.6 g of ethylenimine and 27.3 g of triethylamine in 200 ml of dry benzene was added 24.8 g of the acid chloride of chloromethylphosphinic acid in 100 ml of dry benzene at 0-10°; the mixture was stirred at room temperature for 3-4 hr and left overnight. The triethylamine hydrochloride was removed by filtration, the benzene removed, and the residue distilled; the product had b.p. 84° (0.15 mm). The diimide distilled completely at 10⁻⁴ mm on a bath heated to 80-85°. In an attempt at distillation at 0.25 mm, the product polymerized instantaneously (at a bath temperature of 120°). The yield was 15.7 g (59.0%).

TABLE 2

Formula	Empirical formula	Bath temperature (pressure 10^{-4} mm)	d_4^{20}	n_D^{20}	$M_R D$		Found, %		Calculated %		Yield, %
					found	calc.	P	S	P	S	
$-C_6H_5SCH_2CH_2P(=S)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}S_2N_2P$	110—115°	1.1207	1.5450	74.92	75.02	11.97, 12.10	24.27, 24.16	11.75	24.21	53.0
$-C_6H_5SCH_2CH_2P(=O)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}ON_2SP$	100—115	1.1186	1.5103	66.46	66.70	12.44, 12.57	12.86, 12.95	12.48	12.90	60.0
$-C_6H_5SCH_2CH_2P(=S)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}N_2S_2P$	100—110	1.1394	1.5610	67.32	65.78	13.03, 13.10	26.5, 26.67	13.13	26.23	61.0
$-C_6H_5SCH_2CH_2P(=O)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}ON_2SP$	90—95	1.1689	1.5230	57.47	57.46	13.78, 13.40	13.81, 13.60	14.08	14.54	55.0
$-C_6H_5OCH_2CH_2P(=S)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}ON_2SP$	100—110	1.1271	1.5344	60.78	59.91	14.59, 14.66	—	14.08	—	40.0
$-C_6H_5OCH_2CH_2P(=O)(N<\begin{smallmatrix} CH_3 \\ \\ CH_3 \end{smallmatrix})_2$	$C_{16}H_{17}O_2N_2P$	70—80	1.1822	1.5076	58.55	60.83	13.92, 13.82	—	13.36	—	38.0

The diethylenimide of chloromethylphosphinic acid was a viscous liquid, which crystallized on standing and was soluble in water, benzene, alcohol, chloroform, and acetone.

N,N'-Diethylenimide of S-n-butyl-S-ethylenethiophosphinic acid (typical preparation). a) To 4.35 g of the diethylenimide of vinylthiophosphinic acid were added 2.52 g of butyl mercaptan and a catalytic amount of sodium butylate and the mixture heated at 60° for 10 hr. The excess mercaptan was removed in vacuum and the residual oil distilled at 10^{-4} mm. We obtained the following fractions: 1st fraction at a bath temperature of 60-70°, 1.5 g; 2nd fraction at a bath temperature of 70-90°, 3.5 g (53%). The first fraction was a mixture of the starting material and the final product and the second fraction was the diethylenimide of S-n-butyl-S-ethylenethiophosphinic acid. The substance was a colorless liquid, which was soluble in many organic solvents and insoluble in water.

b) An 8.4 g sample of the diethylenimide of β -chloroethylthiophosphinic acid was added gradually to 4.5 g of freshly prepared sodium n-butyl mercaptide in absolute ether and the mixture stirred at room temperature for 4.5 hr and at the boiling point of ether for 4 hr. The precipitate of NaCl was removed by filtration and washed carefully with ether, the ether removed, and the residue vacuum distilled at a bath temperature of 70-90° (10^{-4} mm). The yield was 7.5 g (71.0%).

N,N'-Diethylenimide of ethoxy- β -ethylthiophosphinic acid. a) A mixture of 4.35 g of the diethylenimide of vinylthiophosphinic acid and 1.56 g of alcohol was heated at 50-60° in the presence of catalytic amounts of sodium ethylate for 20 hr. The excess alcohol was removed in vacuum and the residue vacuum distilled (10^{-4} mm). We obtained the following fractions: 1st fraction at a bath temperature of 70°, 2.4 g, n_D^{20} 1.5390; 2nd fraction at a bath temperature of 100-110°, 2.2 g, n_D^{20} 1.5344. The first fraction was evidently a mixture of the starting material and the ethoxydiimide; the second fraction was the addition product. The yield was 2.2 g (40%). An analogous result was obtained when the reaction was carried out in sealed tubes at 60-65° for 20 hr. The reaction gave a better yield (55%) when the reaction mixture was stirred and heated at 80° for 18-20 hr. The substance was a colorless liquid, which was soluble in organic solvents and sparingly soluble in water. The N,N'-diethylenimide of n-butoxy- β -ethylphosphinic acid was obtained analogously.

b) A 3.5 g sample of the diethylenimide of β -chloroethylphosphinic acid was added gradually to 2.0 g of freshly prepared sodium n-butyl mercaptide in dry ether, the mixture stirred for 5 hr with the ether boiling, the sodium chloride precipitate removed by filtration, the ether removed, and the residue vacuum distilled (10^{-4} mm) at a bath temperature of 70-80°. The yield was 2.34 g (56.0%).

SUMMARY

1. Previously unknown diethylenimides of alkyl- and alkenylthiophosphinic and allylphosphinic acids were prepared.
2. The addition of alcohols and mercaptans to diethylenimides of vinylthiophosphinic and phosphinic acids was studied.

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TRANSESTERIFICATION OF ESTERS OF DIALKYL- AND DIARYLPHOSPHINOUS ACIDS

K. A. Petrov, É. E. Nifant'ev, L. V. Khorkhoyanu,
and A. I. Trushkov

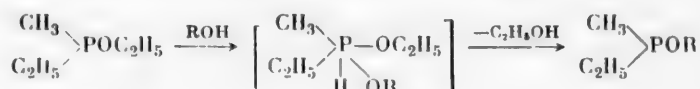
Translated from Zhurnal Obshchei Khimii, Vol. 31, No. 9,
pp. 3085-3090, September, 1961
Original article submitted July 22, 1960

We showed previously that acid esters of methylphosphinous acid are transesterified by monohydric [1] and dihydric [2] alcohols. This method was found to be suitable for the synthesis of various phosphites, including previously unknown ones. The transesterification of neutral phosphites [3], monoalkylphosphinites [4], and acid phosphites [5] by monohydric alcohols has also been studied.

In the present work we studied the transesterification of esters of dialkyl- and diarylphosphinous acids by various alcohols. It was shown that like other esters of acids containing trivalent phosphorus, esters of dialkyl- and diarylphosphinous acids readily undergo this conversion and consequently, all types of acid and neutral esters of phosphorous and phosphinous acids may be used in transesterification.

We made a detailed investigation of the alcoholysis of ethyl methylethylphosphinite.* In contrast to acid phosphonites, esters of dialkylphosphinous acids are transesterified by not only primary and secondary, but also tertiary alcohols. We should note that until now it has not been possible to transesterify esters of acids containing tri- and pentavalent phosphorus with tertiary alcohols and no ester formed by such an alcohol and a phosphinous acid has been known.

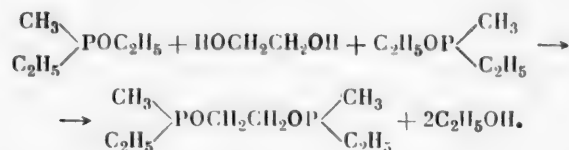
The transesterification of dialkylphosphinous esters proceeds under milder conditions than the transesterification of phosphites and acid phosphinites, for example. This is in accordance with the mechanism of the reaction, which, as was shown previously [1], proceeds through the formation of an intermediate phosphonium compound through the unshared pair of electrons in the electron cloud of the phosphorus atom.



As a result of the lower electrophilicity of the alkyl group in comparison with hydroxyl and alkoxy groups, the electron density at the phosphorus atom in dialkylphosphinous esters is greater than in phosphites and acid methylphosphinites and this facilitates the formation of the phosphonium compound.

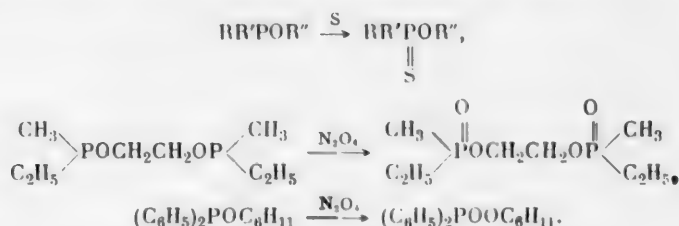
As experiments showed, ethyl diphenylphosphinite undergoes transesterification, but under more drastic conditions; in addition, transesterification could not be effected with tertiary alcohols. These difficulties are caused in the first instance by the high electrophilicity of the phenyl group present in the phosphite and to some extent, by steric hindrance.

In addition to monohydric alcohols, ethylene glycol also reacted with phosphinites to give a satisfactory yield of a neutral biphosphinite:

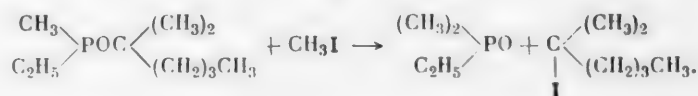


* We obtained ethyl methylethylphosphinite from the corresponding acid chloride, which was obtained by the method in [6].

The esters obtained in the present work (especially esters of secondary and tertiary alcohols) were largely unknown. They were all liquids, which dissolved in organic solvents, were hydrolyzed by water, and were similar in properties to neutral phosphites. They were oxidized readily and added sulfur to form the corresponding derivatives of pentavalent phosphorus, which have not been reported previously in the literature.



When methylethylphosphinites formed by branched alcohols were alkylated, the Arbuzov reaction proceeded smoothly to form a phosphine oxide and the corresponding alkyl halide.



Thus, transesterification proceeds readily with esters of dialkyl- and diarylphosphinous acids. The phosphinites obtained may be used for the synthesis of complex organophosphorus compounds.

EXPERIMENTAL

Ethyl methylethylphosphinite (I). Into a four-necked flask with a stirrer, reflux condenser, thermometer, and dropping funnel were placed 17.7 g of anhydrous alcohol, 114.2 g of freshly distilled diethylaniline, and 350 ml of absolute ether. At 0°, 42.4 g of methylethylchlorophosphine in an equal volume of absolute ether was added dropwise. The mixture was then stirred at room temperature for 1 hr, filtered, and the precipitate washed with absolute ether. The ether was removed and the residue vacuum distilled. All operations had to be carried out in an atmosphere of pure dry nitrogen. We obtained 12.8 g (28%) of product with b.p. 52-58° (100 mm). After redistillation, the substance had the following constants:

B.p. 54-55° (100 mm), n_D^{20} 1.4275, d_4^{20} 0.8755, M_R 35.22; calc. 35.07.

Found %: P 26.25, 26.40. $\text{C}_5\text{H}_{13}\text{PO}$. Calculated %: P 25.80.

It was a colorless, mobile liquid with an unpleasant odor, fumed in air with evolution of heat, dissolved in organic solvents, and was sparingly soluble in water.


Transesterification of ethyl methylethylphosphinite by monohydric alcohols and ethylene glycol. A mixture of alcohol and (I) in a molar ratio of 1 : 1 (a molar ratio of 1 : 3 in transesterification with ethylene glycol) and a small piece of sodium was heated at 120-125° for 3 hr, whereupon ethanol distilled (b.p. 76-78°; yield 90-95%). The mixture was then vacuum distilled. All operations were carried out in an atmosphere of purified nitrogen. The yields of the substances obtained and their constants are given in Table 1.

Transesterification of ethyl diphenylphosphinite (II) by monohydric alcohols. A mixture of (II)* and the alcohol** in a molar ratio of 1 : 1 and a small lump of sodium was heated for 4-5 hr at the boiling point of the starting alcohol (140-190°) until 80-90% of the theoretical amount of alcohol had distilled. The residue was vacuum distilled. All operations were carried out in an atmosphere of purified nitrogen. The yields of the substances and their constants are given in Table 1.

* Ethyl diphenylphosphinite was obtained by the method proposed by A. E. Arbuzov [7] for diphenylchlorophosphine [8].

** Transesterification did not occur with tert-heptanol. Ethanol did not distill and vacuum distillation of the reaction mixture yielded only tert-heptanol [b.p. 40-41° (1 mm), n_D^{20} 1.4162] and ethyl diphenylphosphinite [b.p. 127-128° (1 mm), n_D^{20} 1.5910].

TABLE 1. Synthesis of Diphenyl- and Methylthiophosphinous Esters ($C_6H_5)_2P(OR)$ (I) and $C_2H_5-P(OR)(CH_3)$ (II)

Type	R	Empirical formula	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MRD		% P		Yield, %
						found	calc.	found	calc.	
(I)	$n-C_6H_{13}^*$	$C_{18}H_{20}OPS$	127—128 (0.5)	1.5712	1.0475	89.67	89.30	10.71, 10.69	10.84	80
(I)	$n-C_8H_{17}^{**}$	$C_{20}H_{27}OPS$	160—161 (0.4)	1.5550	1.0180	98.54	98.54	10.07, 10.01	9.87	81
(I)	$n-C_6H_{13}$ 	$C_{18}H_{21}OPS$	161—168 (1)	1.5905	1.0935	87.64	87.10	11.01, 10.91	10.91	83
(II)	$n-C_6H_{13}$	$C_9H_{21}OPS$	72—73 (7)	1.4430	0.8545	54.67	54.94	17.39, 17.37	17.58	50
(II)	$n-C_8H_{17}$	$C_{11}H_{25}OPS$	94—95 (7)	1.4500	0.8584	63.94	64.18	14.91, 15.04	15.17	64
(II)	$sec-C_8H_{17}$	$C_{11}H_{25}OPS$	105—106 (11)	1.4465	0.8517	64.03	64.18	14.90, 14.81	15.17	40
(II)	$(CH_3)_2C-(CH_2)_3CH_3$	$C_{10}H_{23}OPS$	72—73 (9)	1.4430	0.8450	59.61	59.56	16.23, 16.18	16.30	40
(II)	$OCH_2CH_2O^{***}$	$C_9H_{20}O_2P_2$	97—99 (9)	1.4632	0.9665	61.29	61.51	29.07, 29.41	29.52	53

* Literature data [8]: b.p. 138—141° (0.3 mm), n_D^{20} 1.5608, d_4^{20} 1.0140.** Literature data [8]: b.p. 156—162° (0.2 mm), n_D^{20} 1.5508, d_4^{20} 1.0066.

*** Biphosphinite obtained.

TABLE 2. Synthesis of Diphenyl- and Methylthiophosphinic Esters $(C_6H_5)_2P(S)OR$ (I) and $C_2H_5-P(S)OR$ (II)

Type	R	Empirical formula	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MRD		% P		Yield, %
						found	calc.	found	calc.	
(I)	$n-C_6H_{13}^*$	$C_{20}H_{27}OPS$	138.5—139° (0.01)	1.5710	1.0798	105.53	105.40	8.85, 8.71	9.13, 9.11	80
(I)	$sec-C_8H_{17}$	$C_{11}H_{25}OPS$	147—148 (2)	1.4740	0.9477	69.98	70.04	12.81, 12.75	13.35, 13.15	80.5
(II)	$(CH_3)_2C-(CH_2)_3-CH_3$	$C_{10}H_{23}OPS$	126—127 (2)	1.4682	0.9242	66.25	66.42	13.86, 13.57	14.10, 14.01	76.5

* Literature data [8]: b.p. 180—185° (0.2 mm), n_D^{20} 1.5658, d_4^{20} 1.0521.

Addition of sulfur to methylethyl- and diphenylphosphinous esters. The phosphinite was gradually mixed with an equimolecular amount of sulfur and the temperature of the mixture rose to 80-110°; the mixture was heated at 110-115° for 2 hr, cooled, filtered to remove sulfur, and vacuum distilled. The yields and constants of the compounds obtained are given in Table 2.

Glycol ester of methylethylphosphinic acid. Into a flask protected from moisture was placed 1.4 g of the glycol ester of methylethylphosphinous acid and nitrogen oxides in a stream of dry nitrogen passed in with cooling with ice and salt until a green color appeared. The excess nitrogen oxides were removed by flushing the mixture with dry nitrogen and keeping the mixture in vacuum. We obtained 1.6 g of product (almost quantitative yield).

B.p. 117-118° (0.5 mm), n_D^{20} 1.4712.

Found %: P 25.16, 25.48. $C_8H_{20}O_4P_2$. Calculated %: P 25.62.

The thick, viscous, yellow mass was soluble in organic solvents.

Cyclohexyl ester of diphenylphosphinic acid. As described above, from 3.5 g of the cyclohexyl ester of diphenylphosphinous acid we obtained 3.6 g (almost quantitative yield) of product with m.p. 112-112.5° (from ether).

Found %: P 9.83, 9.91. $C_{18}H_{21}O_2P$. Calculated %: P 10.23.

The colorless crystals were readily soluble in dichloroethane, benzene, and alcohol and difficultly soluble in ether.

Arbuzov rearrangement with tert-heptyl methylethylphosphinite. A 1.9 g sample of heptyl methylethylphosphinite was mixed with 1.4 g of methyl iodide (the temperature rose to 70-75°). The mixture was heated on a water bath for 1 hr. On cooling, colorless, lustrous prisms separated and these were collected. The filtrate was vacuum distilled and we collected a fraction with b.p. 95-97.5° (10 mm); the substance crystallized in the receiver. The total yield of dimethylethylphosphine oxide was 0.6 g (56%); m.p. 76-77° (from alcohol). Literature data [9]: m.p. 73-75° and b.p. 223°.

SUMMARY

1. The transesterification of ethyl methylethylphosphinite with primary, secondary, and tertiary alcohols is a convenient method of synthesizing various esters of methylethylphosphinous acid.
2. The transesterification of ethyl diphenylphosphinite with primary and secondary alcohols is a convenient method of synthesizing esters of diphenylphosphinous acid.
3. Ethyl methylethylphosphinite was transesterified with ethylene glycol.
4. Some chemical properties of the phosphinites obtained were studied.

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ON THE MECHANISM OF LACTONE FORMATION IN THE LIQUID -
PHASE AUTOXIDATION OF CERTAIN POLYALKYLBENZENES

R. N. Volkov and S. V. Zavgorodnii

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In the preceding works it was found that in the autoxidation of various polyalkylbenzenes containing adjacent methyl and isopropyl groups, γ -lactones - 3,3-dimethylphthalide and its homologs - are formed [1, 2].

The autoxidation of o-cymene was studied earlier [3]; however, 3,3-dimethylphthalide was not found among the oxidation products in this case.

In order to investigate the kinetics and chemism of lactone formation in detail, the autoxidation of 2-isopropyl-p-xylene (I) and 2,5-diisopropyl-p-xylene (II) was studied in the present work.

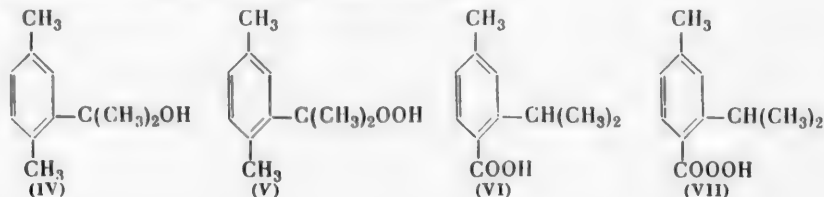
In the presence of manganese resinate the oxidation of hydrocarbon (I) by atmospheric oxygen goes very slowly, apparently owing to steric hindrances arising in the attack of the peroxide radical on the blocked groups, which in the transition state cannot assume the degree of coplanarity attained in compounds not containing substituents in the ortho-position. Owing to the low conjugation energy the total rate of oxidation of both blocked groups is only 30 to 70% greater than the rate of oxidation of the methyl group standing alone, whereas the isopropyl group in 4-isopropyl-o-xylene, for instance, is four times as reactive as the methyl [2]. (Adjacent methyl groups do not give rise to steric hindrance: o-Xylene is oxidized more readily than the meta- and para-isomers). On studying the joint oxidation of hydrocarbon (I) and p-xylene, we found that the latter is only 23% less reactive. It is interesting to note that according to the cited data [3], o-cymene is oxidized half as fast as p-cymene. However, these authors gave an excessively high value for the reactivity of the ortho-isomer, since the o-cymene used by them was prepared by alkylation of toluene with isopropyl alcohol, and undoubtedly contained considerable amounts of other isomers.

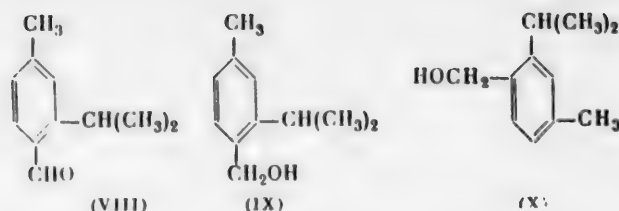
The oxidation of hydrocarbon (II) goes much faster than that of (I). This is due not only to the somewhat higher relative reactivity of hydrocarbon (II) toward free radicals, but also to the fact that in the given case less-stable primary hydroperoxides are obtained, which easily decompose to acids which slow the oxidation. The negative effect of the methyl group on the rate of chain growth probably is even more important. It is well known, for instance, that p-cymene is oxidized more slowly than cumene, although the methyl and isopropyl groups activate one another [4].

In the presence of more active initiators - cobalt acetate and isopropyltoluate - hydrocarbons (I) and (II) are oxidized faster than with manganese resinate (owing to degenerate branching), but in this case, naturally, the main reaction products are not hydroperoxides, but the alcohols, ketones, acids, lactones, and the like, resulting from their decomposition.

The kinetics of accumulation of the oxidation products of hydrocarbon (I) in the presence of 1 mole % of cobalt isopropyltoluate, is shown in Figs. 1-4. From these data it is evident that lactones begin to accumulate in the mixture in the earliest stages of the reaction.

Assuming that lactone formation is a strictly consecutive process, 3,3,5-trimethylphthalide (III), for instance, can be obtained only by oxidizing the following substances (IV-X).





Equations, describing consecutive reactions [5], conclusively show that the rate of lactone accumulation, observed in practice, is possible only when the blocked alkyl groups in compounds (IV-X) are oxidized several times as fast as the original hydrocarbon as a whole. From the point of view of ideas on the polarization of the transition state [4, 6] this situation is improbable, since electronegative substituents, on the contrary, should hinder oxidation. However, the reactivity of hydrogen atoms depends not only on polar effects, but also on other factors, e.g., the energy of cleavage of the corresponding C-H bonds. It is difficult to foresee how the latter quantity will vary in compounds (IV-X) and which factor will be decisive, since concrete data on the effect of analogous substituents, located in the ortho-position relative to the reaching group, do not occur in the literature.

Numerous examples indicate that the effect of polar substituents is often manifested very specifically. For instance, the hydroxyl and hydroperoxide groups increase the activity toward peroxide radicals, of hydrogen atoms bound to the same carbon atom as the OH or OOH group; chloro derivatives of methane are chlorinated more readily than methane, etc. On the other hand, however, ethyl chloride is much more difficult to chlorinate than ethane [7]; on treatment of isobutyric acid with chlorine, hydrogen is detached from the primary, and not the tertiary carbon atom, although the bond strength is much less for the latter [6].

We experimentally tested the possibility of lactone formation according to the usual consecutive scheme, i.e., from substances (IV-X).

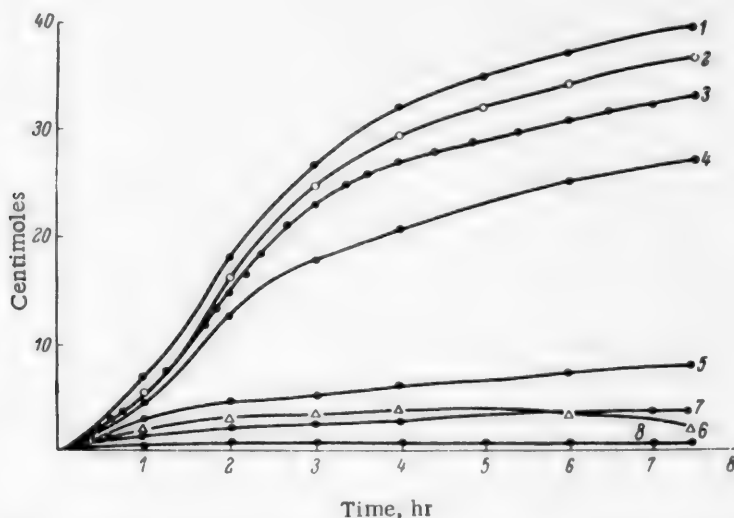


Fig. 1. Kinetics of accumulation of isopropyl-p-xylene oxidation products at 160°. 1) Water (ml/mole); 2) acids; 3) total quantity of lactones; 4) trimethylphthalide; 5) ketones; 6) primary alcohols; 7) tert. alcohols; 8) hydroperoxides.

Oxidation of synthetic alcohol (IV) gave 3,3,5-trimethylphthalide (III), which was identical with the substance formed directly from hydrocarbon (I), but the yield of (III), reckoned on the oxidized alcohol, was only 30%. The rate of oxidation of pure (IV) was much smaller than that for hydrocarbon (I). Other derivatives, found in the reaction mass: 2-acetyl-p-xylene (XI), acids and primary alcohols, also are oxidized more slowly than hydrocarbon (I). The

oxidation products of the indicated compounds are not all lactones by any means in this case. On the one hand, peroxide and other radicals react with the sterically unhindered group to a considerable degree, whereas on the other, even the oxidation of adjacent groups leads in part to the formation of keto alcohols, diols, keto acids, and the like.

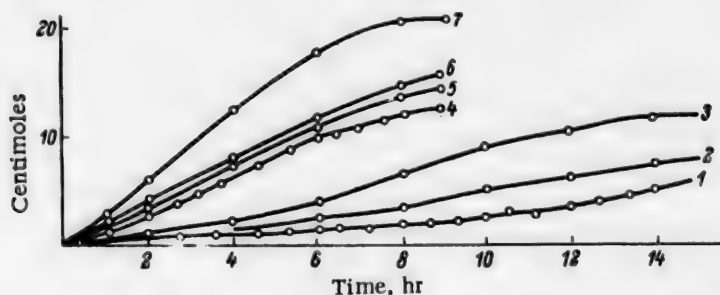


Fig. 2. Oxidation of isopropyl-p-xylene at 110°. With addition of 18% of dimethylxylylcarbinol (IV: 1) Water (ml/mole); 2) trimethylphthalide; 3) acids. Without such addition: 4) water; 5) trimethylphthalide; 6) total quantity of lactones; 7) acids.

Of course, the low rate of oxidation of the intermediate compounds taken individually, is not necessarily a reliable proof that they also are oxidized more slowly than the hydrocarbon, in the reaction mixture.

In the oxidation of a mixture of substances the ratio of rate constants for competing reactions is determined by the reactivity of the components toward the free radicals and does not depend on the rate of propagation of peroxide

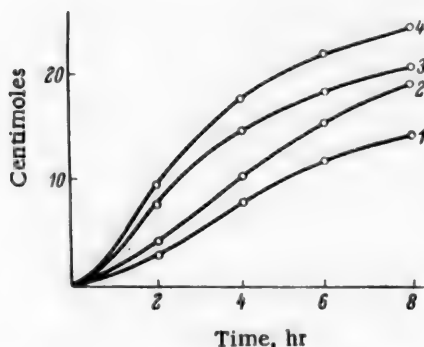


Fig. 3. Oxidation of isopropyl-p-xylene at 130°. With addition of 14% of acetyl-p-xylene (XI): 1) Acids; 2) lactones. Without such addition; 3) lactones; 4) acids.

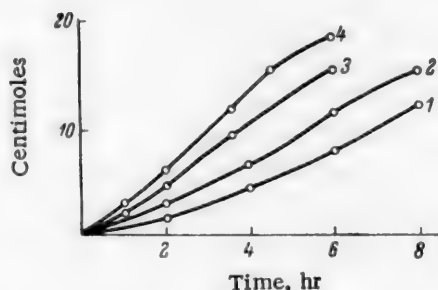


Fig. 4. Oxidation of isopropyl-p-xylene at 130° with additions of isopropylxylylcarbinols and isopropyltoluic acids. Addition of 20% of acids (VI) and (XIV): 1) Acid accumulation; 2) lactone accumulation. Addition of 10% of primary alcohols (IX) and (XV): 3) lactones; 4) acids.

radicals, the presence of inhibitors, or the like. In the oxidation of the individual compounds these factors may be decisive. Therefore we also carried out the joint oxidation of substances (IV), (XI), and p-xylene and studied the effect of additions of compounds (IV), (VI), (IX), and (XI) on the kinetics of lactone accumulation. It was found that the rates of oxidation of compounds (IV), (XI), and p-xylene are nearly the same, and therefore compounds (IV) and (XI) are less reactive than hydrocarbon (I).

As is evident from Figs. 2-4, additions of the substances indicated above do not increase the yield of lactones. Finally, if the latter were obtained mainly by fast oxidation of compounds (V), (VII), and (X), the yield of lactones

Scheme of oxidation of 2-isopropyl-p-xylene

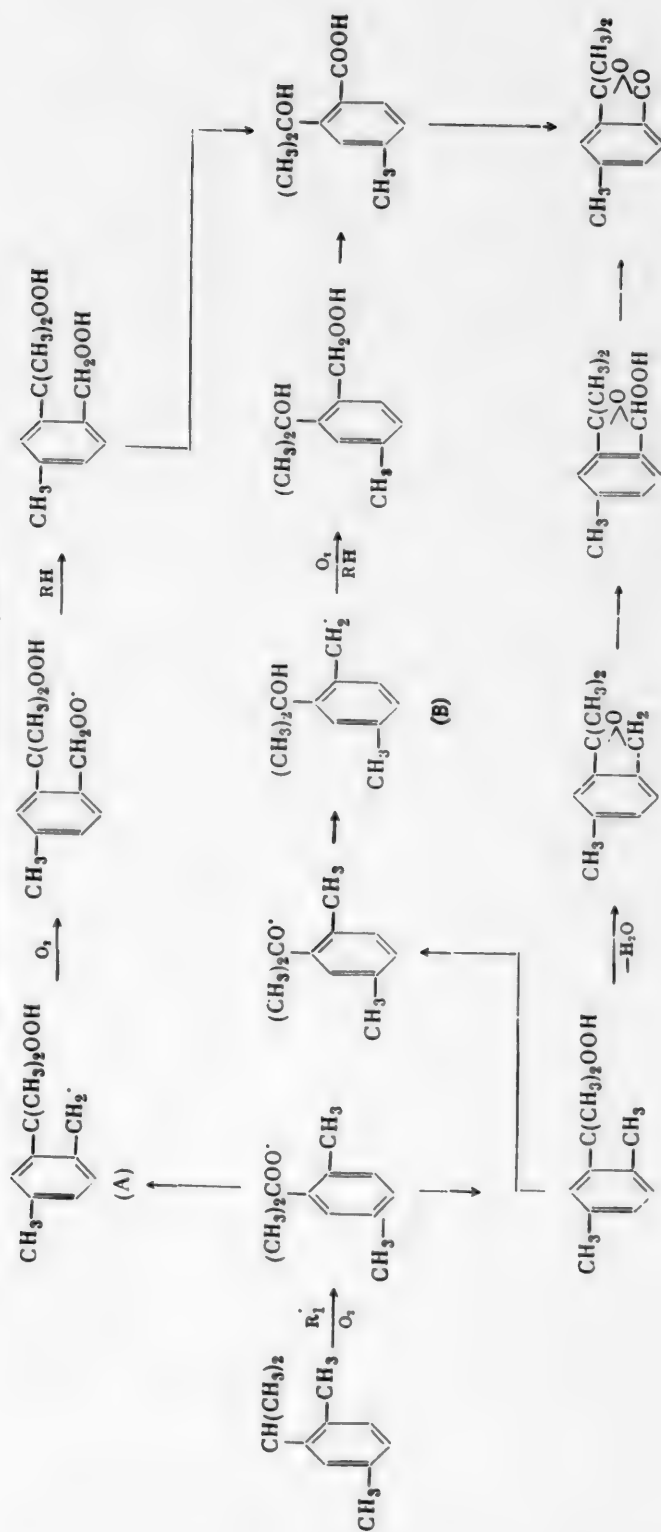


TABLE 1. Autoxidation of 2-Isopropyl-p-xylene (Experiments 1-5) and 2,5-Diisopropyl-p-xylene (Experiments 6 and 7)

Expt. no.	Cobalt isopropyl-toluate taken (mole, %)	Temperature	Hydroperoxide concentration (in %) (numerator); time (in hr) (denominator)	Yield, reckoned on the hydrocarbon taken (mole %)							Hydrocarbon re-generated (in %)
				derivatives of 3,3-di-methylph-	other	lactones	acids	tert. alcohols	ketones	prim. alcohols	
1 *	—	110°	1.2/5, 3.5/12, 1.0/24	4.8	0.8	—	8.3	2.9	2.0	2.6	70.2
2	0.6	110	2.0/1, 3.8/3, 1.6/9	14.0	2.1	—	20.5	4.2	3.5	5.0	46.5
3	1.5	115	1.3/4, 1.7/6, 0.5/14	12.6	3.0	—	25.8	2.7	4.1	3.3	42.0
4	1.0	125	0.6/1, 0.9/2,	5.1	1.2	—	4.3	2.9	1.8	1.9	77.6
5	1.1	140	0.4/1, 0.5/3, 0.3/5	16.3	4.4	—	26.2	4.3	6.1	2.7	33.5
6	1.0	120	1.8/1, 0.7/3, 0.6/4	25.6	3.8	—	5.1	4.0	5.3	3.5	38.4
7 *	—	110	4.0/2, 10.3/7, 1.5/18	21.7	4.1	—	4.3	5.2	2.6	1.9	43.3

* Ten mM of manganese resinate and 3 moles of soda were used in Experiment 1, and 6 mM of manganese resinate and 10 moles of soda in Experiment 7.

and other substances with two oxidized alkyl groups would vary directly with the hydroperoxide concentration in the reaction mass. Actually, as is evident from the data of Table 1, such a direct relation between the indicated quantities does not exist.

Obviously the process of lactone formation is mainly based not on consecutive intermolecular reactions, but on intramolecular conversions of intermediate products — free radicals and hydroperoxides.

Three principal routes of intramolecular conversion are theoretically possible: isomerization of free peroxide radicals, oxidation of adjacent alkyl group by a monohydroperoxide, and isomerization of alcohol radicals. For one of the special cases the indicated process may be represented by the following scheme (see diagram).

As is well known, unimolecular reactions have a preexponential factor 10^{23} times as great as bimolecular [8]. If the activation energies of these reactions were equal, the unimolecular process would go about 100 times as fast as the bimolecular, even in the liquid phase. Practically, for steric reasons, the difference between the activation energies of competing intramolecular and bimolecular reactions must be a positive quantity. According to approximate quantum-mechanical calculations the attack of the σ -bond is most effective at an angle equal to zero [8], which is more easily achieved in intermolecular reactions. However, even at $\Delta E = 2800-3600$ cal and 120° the ratio of rates for the intramolecular and bimolecular processes is 1 : 1/6.

At first glance it may appear that that effect, due to isomerization of peroxide and alcohol radicals, will be small, since radicals (A) and (B) detach a hydrogen atom from the surrounding molecules before oxygen adds on to them, the concentration of the latter in the mixture being about 10^{-3} M. However, benzyl-type radicals are so stable that they detach practically no hydrogen atoms even from such active hydrocarbons as cumene and cyclohexene [9]. For the structurally-similar styrene radicals the rate constant for oxygen addition is of the order of $10^6 - 10^7$ liters/mole·sec, whereas the rate constants for detachment of hydrogen from toluene and cumene are 0.0024 and 0.016 liter/mole·sec, respectively [6]. Hence most of the radicals, obtained as a result of isomerization, will react with oxygen and will give lactones and other substances with oxidized adjacent groups.

In order to find out which of the three routes of lactone formation is the principal one, we performed the following experiments. By oxidizing hydrocarbon (II) at 110° in the presence of the least possible amount of manganese resinate and soda, we obtained a reaction mass containing 9% hydroperoxides. After reduction of the latter with sulfite and analysis of the mixture it was found that only a small amount of products with two oxidized alkyl groups is formed in the given case.

We then studied the thermal decomposition of 9% hydroperoxide in the absence of oxygen. In this case the reaction products included not only acids, lactones, alcohols, and ketones, but also a small amount of an inert substance which on distillation passed into the alcohol and ketone fractions, as a result of which the sum of their con-

centration was 8-10 units less than 100%. We assume that the indicated inert substance was 1,1,6-trimethyl-5-isopropylphthalane. Since decomposition of the hydroperoxides gives little of this substance, it is quite obvious that the intramolecular conversion of monohydroperoxides to phthalans, like the isomerization of peroxide radicals, is not the principal cause of lactone formation.

When the hydroperoxides were decomposed in the presence of oxygen, 3,3,5-trimethyl-6-isopropylphthalide was obtained in approximately 50% yield (reckoned on the oxidized hydrocarbon); the same lactone yield was obtained when hydrocarbon (II) was oxidized with cobalt *o*-isopropyltoluate.

Therefore lactones are obtained mainly through the isomerization of alcohol radicals (see the scheme given above). The indicated mechanism well explains the absence in the reaction mass, of significant quantities of keto acids and other compounds with two oxidized alkyl groups, aside from homologs of 3,3-dimethylphthalide, and also the fact that under severe conditions lactones are formed practically with no induction period. If lactones were obtained mainly through the *o*-dihydroperoxide, the keto-acid concentration in the mixture could not be much less than the concentration of 3,3-dimethylphthalide derivatives, since the decomposition of tertiary hydroperoxides usually gives a considerable amount of ketones along with the alcohols. The scheme, based on the intermediate formation of phthalans, is free from the last contradiction but fails to explain a number of substantial regularities, e.g., the fact that in the presence of cobalt salts, which easily decompose hydroperoxides with the formation of alcohol radicals, the lactone yield not only is not decreased, but often is even increased.

The causes of the low yield of lactones on oxidation of *o*-xylene and 4-isopropyl-*o*-xylene may be explained on the basis of the hypothesis on the principal mechanism of lactone formation, advanced earlier [1, 2]. As is well known, primary hydroperoxides, contrary to tertiary, decompose very readily according to the scheme



For this reason the amount of isomerizable alcohol radicals $\text{RCH}_2\text{O}^\cdot$, obtained from the hydroperoxide, is diminished.

The oxidation of hydrocarbons (I) and (II) gives not only derivatives of 3,3-dimethylphthalide, but also other substances which are readily hydrolyzed by alkali but, contrary to 3,3-dimethylphthalides, are regenerated from the alkali salts in the form of neutral compounds only after boiling in an acid medium. Phthalide and its homologs (substituted in the nucleus) have such properties, as was pointed out earlier [1, 2]. These lactones could not be isolated in the form of individual compounds; however, since their oxidation gave 4-methyl-*o*-phthalic acid, they obviously were substances with two oxidized adjacent groups. Lactone-type compounds also are formed in the autoxidation of acetylxylene (XI) in 20-28% yields, reckoned on the oxidized product. Lactones were found also in tars and high-boiling products. Possibly they were formed through the polymerization of unsaturated lactones, and conversions of *o*-keto acids [10].

The optimum temperature for synthesizing homologs of 3,3-dimethylphthalide is 130-140°. A great deal of by-products and tars is obtained at higher temperatures.

EXPERIMENTAL

2-Isopropyl-*p*-xylene (I), b.p. 196°, n_D^{20} 1.5010, d_4^{20} 0.8762 and 2,5-diisopropyl-*p*-xylene (II), b.p. 244°, m.p. 37.4°, were prepared by alkylating *p*-xylene with propylene [11]. 2-Acetyl-*p*-xylene (XI), b.p. 110° (10 mm), n_D^{20} 1.5306, was synthesized from *p*-xylene and acetyl chloride in the presence of AlCl_3 . Dimethyl-*p*-xylylcarbinol (IV), b.p. 98° (3 mm), m.p. 40°, was prepared by the Grignard reaction from acetone and 2-bromo-*p*-xylene. The latter was prepared by brominating *p*-xylene in the presence of iron; b.p. 205°, n_D^{20} 1.5503, d_4^{20} 1.3557.

Autoxidation and analysis of the reaction products were carried out as in the preceding works [1, 2]. Usually 0.8-1 mole of hydrocarbon (I) and 0.2-0.3 mole of (II) were taken for the experiment.

The main oxidation products of hydrocarbon (I) were: 4-methyl-3-isopropylbenzoic acid (XIV), m.p. 147° (from benzene); 3,3,5-trimethylphthalide (III), b.p. 297°, m.p. 92° (from petroleum ether); 2,5-dimethylacetophenone (XI), semicarbazone and 2,4-dinitrophenylhydrazone m.p. 168 and 175°, respectively; 4-methyl-2-isopropylbenzoic acid (VI); dimethyl-*p*-xylylcarbinol (IV); 4-methyl-3-isopropylbenzyl (XV) and 4-methyl-2-isopropylbenzyl (IX) alcohols. Yields of the indicated products are given in Table 1. The structure of acid (XIV) was established by oxidizing it to trimellitic acid (m.p. 228-232°), decarboxylation to *o*-cymene, and determination of the elementary composition and neutralization equivalent.

TABLE 2

Substance oxidized	Quantity (g)	Temperature	Time (in hr)	Yield, %	
				lactones	acids
Dimethyloxylcarbinol (IV)	25.6	120°	28	2.9	6.3
Acetylxylene (XI)	64.7	120	10	7.2	23.7
Isopropyltoluic acids (VI) and (XIV)	28.0	130	20	0.5	0.6
Isopropyltolylcarbinols (XV) and (IX)	12.0	110	10	1.1	18.6

TABLE 3

	Composition of the reaction mass (in %) in experiment			
	1	2	3	4
3,3,5-Trimethyl-6-isopropylphthalide	1.6	1.9	15.7	5.6
4-Methyl-2,5-diisopropylbenzoic acid	1.2	2.0	3.9	0.9
Fraction with b.p. 100-125° (2 mm)	7.6	7.2	10.5	2.0
Content in it of:	ketones	1.9	21.0	26.4
	tert. alcohols	81.2	62.9	57.7
	prim. alcohols	13.5	6.3	11.8
	unidentified products	3.4	9.8	4.1
Fraction with b.p. 125° (2 mm) (diols, ketoalcohols)	1.1	0.9	1.6	0.5
Keto acids	—	0.2	1.3	—

Found %: C 74.42; H 7.74. M 178.4. $C_{11}H_{14}O_2$. Calculated %: C 74.13; H 7.92. M 178.2

o-Cymene had constants corresponding to the pure, synthetic product [12]: b.p. 177°, n_D^{20} 1.5010, d_4^{20} 0.8790. Oxidation of *o*-cymene with nitric acid in an autoclave gave *o*-phthalic acid; melting point of anhydride, 131°. Acid (VI) was not isolated in pure form. The relative contents of acids (XIV) and (VI) in the acid mixture were 80 and 20%, respectively; the relative amounts of primary alcohols (XV) and (IX) were about the same. The structures of substances (VI), (XV), and (IX) were proved similarly [2]. Dimethyl isophthalate had m.p. 67°. *o*-Phthalic acid was separated from isophthalic acid by using its high solubility in cold water, and also by sublimation in the form of the anhydride.

Tertiary alcohol (IV) could not be isolated from the reaction mass in the individual state. Dehydration of alcohol (IV) gave 2,5-dimethylisopropenylbenzene, which was converted by oxidation to ketone (XI) and 2,5-dimethylbenzoic acid, m.p. 133°.

Lactone (III) was oxidized with 25% nitric acid in an autoclave to trimellitic acid; cleavage of (III) with potassium hydroxide at 200° gave acetone (2,4-dinitrophenylhydrazones m.p. 123-125°) and *p*-toluic acid, m.p. 180°. The composition of (III) was confirmed by elementary analysis and molecular-weight determination.

Found %: C 74.72; H 7.02. M 174.7 (cryoscopy in benzene), 176.4 (back-titration). $C_{11}H_{12}O_2$. Calculated %: C 74.98; H 6.87. M 176.2.

The amounts of the oxidation products of (II) were determined by methods adopted by us earlier [1, 2]; the structure of the substances, except 3,3,5-trimethyl-6-isopropylphthalide (XVI), was not specially determined. (owing to the symmetrical structure of the hydrocarbon that was oxidized, the primary and tertiary alcohols and ketones could not have isomers.).

The ring of lactone (XVI) was opened with somewhat more difficulty by treatment with alkali than in the case of (III) and other trialkylphthalides. The quantitative conversion of (XVI) to the hydroxy-acid salt required heating for 2-3 hr or 10-15 days' contact with an excess of 1 N KOH at room temperature. The quantitative determination

of (XVI) in various mixtures could be carried out by the method described earlier [2]. In the given case, however, the excess alkali had to be titrated still more cautiously. It was best to neutralize at a temperature below -20° , diluting the mixture beforehand with methanol, and to use an alcoholic solution of benzoic or acetic acid for titration. (For instance, about 25% of the hydroxy-acid salt was converted to the lactone on titration with sulfuric acid at 20° , which markedly lowered the results.).

M (XVI) (by titration) 219.8. $C_{14}H_{18}O_2$. Calculated M 218.3.

Decomposition of (XVI) with alkali at $200-230^{\circ}$ gave acetone and acid (XIV), m.p. $146-147^{\circ}$, which proved the structure of the lactone. Besides (XVI), m.p. 85° , b.p. 165° (10 mm), an acid, which obviously was 4-methyl-2,5-diisopropylbenzoic acid, m.p. 129° , was isolated in pure form from the oxidation products of (II).

M 220.6. $C_{14}H_{20}O_2$. Calculated M 220.3.

Results of experiments in oxidation of the presumed intermediate products of lactone (III) synthesis in the presence of 1 mole % of cobalt isopropyltoluate are given in Table 2.

For the indicated experiments synthetic alcohols (IV) and (XI), an acid mixture containing approximately-equal quantities of acids (VI) and (XIV), and a primary-alcohol mixture containing 80% (XV) and 20% (IX), were used. These substances were employed as additions to hydrocarbon (I). The composition of the oxidation products of (II) is given in Table 3.

In Experiment 1 the reaction mass, obtained by oxidation of (II) at 110° in the presence of 5 mM of manganese resinate up to a hydroperoxide concentration of 9%, was reduced with sulfite. In Experiment 2 the same hydroperoxide in 3% concentration was decomposed at 125° in the absence of oxygen. In Experiment 3 further oxidation was carried out at 125° until the hydroperoxides were almost completely destroyed. Under Experiment 4 the composition of a mixture, oxidized approximately to the same degree as in the first two experiments, in the presence of 1 mole % of cobalt isopropyltoluate, is given for comparison.

SUMMARY

The regularities of autoxidation of 2-isopropyl-p-xylene and 2,5-diisopropyl-p-xylene in the presence of cobalt and manganese salts, were studied. It was shown on the basis of kinetic data, that the main cause of high lactone yields is the isomerization of alcohol radicals, accompanied by detachment of a hydrogen atom from an adjacent alkyl group.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

INVESTIGATION OF CERTAIN PROPERTIES OF ALKYL- CHLOROSILANES IN AN ACETONITRILE MEDIUM

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Alkylchlorosilanes are the principal raw material for synthesizing organosilicon compounds of high molecular weight, which are distinguished by valuable technical properties [1]. However, despite the great importance of alkylchlorosilanes, their physicochemical properties have not been sufficiently studied. This is explained by the fact that alkylchlorosilanes are extremely sensitive to water, which causes them to decompose with the formation of the corresponding silanols; the latter are condensed to polysiloxanes.

Hydrolytic cleavage of alkylchlorosilanes takes place readily even in the presence of atmospheric moisture. Since investigation of the properties of alkylchlorosilanes is extremely difficult, the study of their properties in non-aqueous media is of great theoretical interest.

Abrahamson and Reynolds [2] conducted a polarographic investigation of alkyl- (or aryl)chlorosilanes in aqueous-pyridine solution (volume ratios from 3 : 7 to 1 : 1). In this case the Si-Cl bond was hydrolytically cleaved, and the pyridinium ion, formed through the interaction of alkylchlorosilane hydrolysis products and pyridine, was reduced at the dropping-mercury cathode. The polarography recorded the result of irreversible chemical changes of alkylchlorosilanes, and not the true behavior of alkylchlorosilanes at the dropping-mercury cathode. An investigation of alkylchlorosilanes by the potentiometric method is described in [3].

In the present article an investigation of methylchlorosilanes by the conductometric method is described. They were conductometrically titrated in solution in a number of organic solvents, and the specific and equivalent electrical conductivities of individual methylchlorosilanes were measured in acetonitrile. The choice of acetonitrile as solvent was determined by a number of its characteristics. Firstly, acetonitrile is an excellent solvent for many inorganic, organic, and organosilicon compounds; secondly, it causes increased dissociation of salts, acids, and bases in many cases; thirdly, association in the liquid state is less in acetonitrile than in many other solvents, e.g., methanol and ethanol (the Trouton constants are equal to 20.1, 24.9, and 26.5, respectively). With respect to numerous compounds which have unshared electrons, acetonitrile behaves like an acid. On interaction with Lewis acids acetonitrile displays basic properties. The tendency of acetonitrile to lose an electron is less marked than that of such nitrogen-containing solvents as pyridine (the corresponding ionization potentials are 11.96 and 9.8 eV).

According to Mulliken's donor-acceptor classification [4], acetonitrile can function in two ways: as an onium electron donor (a base containing a relatively easily-ionized unshared electron pair) and as a π -ketoid acceptor (interaction amounts to the formation of one σ -bond and cleavage of one π -bond).

The investigation confirmed some of our theoretical premises, determined by the above-indicated properties of acetonitrile, in which medium the alkylchlorosilanes behave like weak acids.

EXPERIMENTAL

Trimethylchlorosilane, dimethyldichlorosilane, and methyltrichlorosilane constituted the subject of our investigation. All compounds to be tested were purified by repeated distillation and had physicochemical constants corresponding to literature data.

Organic bases, containing tertiary nitrogen atoms (pyridine, quinoline, 8-hydroxyquinoline, dimethylaminoantipyrine, etc.), were tested as titrants.

Commercial acetonitrile was purified by the method, proposed by Walden and Birr [5] and intended for the preparation of acetonitrile with constant electrical conductivity.

To carry out the conductometric titration a Kohlrausch bridge was assembled. Instead of a resistance box and slide wire, an R-38 rheochord resistance bridge, which is a balanced single bridge with a comparison arm having stepwise control and a continuously-variable arm ratio, was connected into the system. High-frequency (1000 cycle) alternating current was supplied to the system by a ZG-1 sound generator. A Type INO-3M (1957) oscillographic indicator was used for visual indication of bridge balance. A horizontal straight of minimum thickness on the oscillograph screen corresponded to perfect bridge balance.

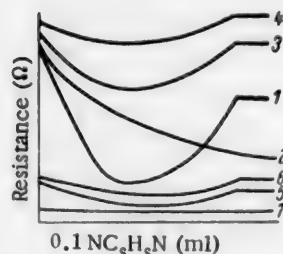


Fig. 1. Conductometric-titration curves of trimethylchlorosilane with pyridine in various organic solvents. 1) Acetonitrile; 2) benzonitrile; 3) nitromethane; 4) nitrobenzene; 5) cyclohexanone; 6) methyl ethyl ketone; 7) methyl butyl ketone.

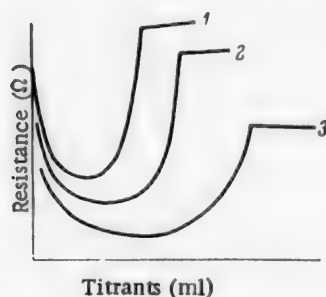


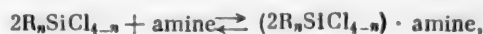
Fig. 2. Conductometric-titration curves of methylchlorosilanes with dimethylaminoantipyrine in acetonitrile. 1) $(\text{CH}_3)_3\text{SiCl}$; 2) $(\text{CH}_3)_2\text{SiCl}_2$; 3) CH_3SiCl_3 .

(0.5% acetonitrile solution) from colorless to bright - lemon - yellow, coincides with the end point of the titration.

On interaction with organic bases, methylchlorosilanes behave like acids, much as acetic acid behaves on titration with diethylamine or butylamine in chloroform or carbon tetrachloride.

In this reaction the compound $(\text{CH}_3\text{COOH})_2$ - amine is formed first, whereas $(\text{CH}_3\text{COOH} - \text{amine})_2$ is formed when more amine is added [6]. The reaction mechanism was proved spectrophotometrically.

The analogous chemical processes for methylchlorosilanes and organic bases may be represented as follows: The reaction



where "amine" is an organic base (titrant), is completed at the minimum point. From there to the equivalence point the process goes according to the following scheme:



The formation of a complex of general formula $2R_nSiCl_4 \cdot n \cdot \text{amine}$ leads to an increase in the conductivity of the solution being analyzed, which probably is due to dissociation of the complex. On the other hand, the complex $R_nSiCl_4 \cdot n \cdot \text{amine}$ is a more stable compound; this leads to an increase in the solution resistance, due to the decrease in the conductivity of the system being analyzed.

If the equilibrium constants of the first and second processes were equal, the minimum on the curve would correspond to titration of exactly half the amount of the original methylchlorosilane. It is evident from the figures that K_1 is greater than K_2 .

The fact, that the titration of alkylchlorosilanes with the chosen organic bases goes according to the proposed scheme, may be proved by analyzing conductometric-titration curves of alkylchlorosilanes with an organic base and an organic base with an alkylchlorosilane (Fig. 3). On titrating a base with a methylchlorosilane up to the equivalence point we have an excess of the base, which leads directly to formation of the final reaction product.

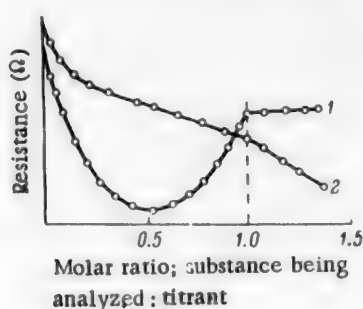


Fig. 3. Conductometric-titration curves of trimethylchlorosilane with pyridine (1) and pyridine with trimethylchlorosilane (2).

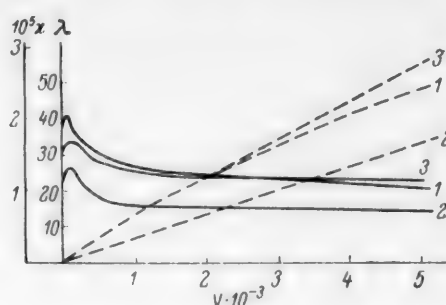


Fig. 4. Dependence of the specific conductivity (κ) and equivalent conductivity (λ) (dashed lines) on the degree of dilution for acetonitrile solutions of methylchlorosilanes. 1) $(CH_3)_3SiCl_2$; 2) $(CH_3)_2SiCl_2$; 3) CH_3SiCl_3 .

In order to establish the possibility of electrolytic dissociation of the methylchlorosilanes themselves, we measured the conductivity of methylchlorosilanes in acetonitrile at constant temperature (26°). The character of the change in the specific and equivalent conductivities of methylchlorosilanes with dilution of their acetonitrile solutions is shown in Fig. 4. As is evident from this figure, λ increases with the degree of dilution of the methylchlorosilane solutions; this is due to an increase in the degree of dissociation (α) of the methylchlorosilanes. On the basis of the dependence of λ on the degree of dilution, it may be assumed that methylchlorosilanes in nonaqueous media are weak electrolytes and are governed by Ostwald's law.

The scheme of formation of conducting acetonitrile solutions of alkylchlorosilanes may be represented, in the case of trimethylchlorosilane, as follows.

First, acid-base interaction of the nitrile and trimethylchlorosilane takes place, leading to the formation of a so-called "outer" complex:



As a result of charge redistribution the "outer" complex then goes over to an "inner" complex:



Finally the "inner" complex may dissociate with the formation of solvated ions according to the equation:



Knowing the mobilities of the ions, into which methylchlorosilanes dissolved in acetonitrile dissociate, one can calculate the dissociation constant for each methylchlorosilane.

The positions of the maxima on the curves of dependence of κ on the degree of dilution for methylchlorosilanes, were distributed regularly, which may give an indirect indication for determining the "strength" of one methylchlorosilane relative to the others. The more the maximum is shifted toward higher methylchlorosilane concentrations, the greater is the "strength" of the methylchlorosilane. Trimethylchlorosilane is the most dissociated, methyltrichlorosilane is the least, and dimethyldichlorosilane occupies an intermediate position.

SUMMARY

1. The interaction of methylchlorosilanes and certain organic bases (pyridine, quinoline, 8-hydroxyquinoline, and dimethylaminoantipyrine) in an acetonitrile medium was studied by the conductometric method.

2. The dependence of the specific and equivalent electrical conductivities of methylchlorosilanes in an acetonitrile medium on the degree of dilution, was determined. It follows from the character of the curves of specific and equivalent conductivity for methylchlorosilanes, that in an acetonitrile medium methylchlorosilanes behave like weak electrolytes in aqueous solutions. The degree of their dissociation decreases in the following order: trimethylchlorosilane > dimethyldichlorosilane > methyltrichlorosilane.

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SYNTHESIS OF ALKYLPHENOLS BY REARRANGEMENT
OF ALKYLPHENYLBORATES IN THE PRESENCE
OF ION EXCHANGE RESINS

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One of these authors synthesized alkylphenols by rearrangement of alkyl arylborates in the presence of catalytic quantities of sulfuric acid [1], followed by hydrolysis. Phenol can be alkylated in the presence of strong cationites [2]. In this work we studied the application of cationites instead of sulfuric acid to the synthesis of alkylphenols from alkyl phenyl borates. The reaction proceeds best in the presence of cationite KU-2 in the acid form (sulfonated co-polymer of styrene and divinylbenzene [3]). Weak cationites are ineffective. The yields are greater than when sulfuric acid is used and sometime ortho-alkylphenols (see table) are also formed. As in the presence of sulfuric acid [1], a parallel side reaction occurs, namely the splitting off of borate to form an alkene. The radicals isomerize on alkylation: n-butyl and propyl - to secondary butyl and isopropyl, isobutyl and isoamyl - to tertiary butyl and tertiary amyl. Plain alkylation of triphenyl borate with trialkyl borate under the same conditions gives much poorer results. We tried to get the least possible di- and polyalkylphenols as was plausible when the starting material used was alkyl diphenyl borate, i.e., when there was a deficiency of alkylating agent. Since the hydroxyl group of phenol was "shielded" during alkylation, the phenols obtained had no non-phenolic impurities. It was noted that under the reaction conditions the cationite KU-2 partially decomposed.

EXPERIMENTAL

Propyldiphenylborate was prepared from 94 g phenol, 30 g propanol, and 31 g boric acid in the presence of 30 ml benzene, as described in [1].

Synthesis of isopropylphenols. To the propyldiphenylborate prepared as above was added 5 g cationite KU-2 (in the acid form) and the mixture was boiled until no more water separated. Gases escaping through the condenser were absorbed in bromine water in two Tishchenko flasks. After 4.5 hours 4.8 ml water was distilled off; the temperature was gradually raised from 177 to 185°; the mixture darkened and became viscous. To it was added 200 ml of 7% NaCl solution, and all boiled for one hour. The liquid was filtered on a heated funnel to separate the cationite. The filtrate was cooled, the oily layer twice extracted with 40 ml benzene, the precipitated boric acid filtered, and the filtrate again extracted with 20 ml benzene. The benzene extracts were combined, washed with a 3% solution of soda and water, dried with calcined magnesium sulfate, the benzene distilled off, and the phenols vacuum distilled from a Favorski flask provided with a 10 cm high fractionating column. This yielded 65.2 g of refluxed phenol and 23.1 g isopropylphenols, b.p. 116-145° (50 mm). The mixture of isopropylphenols thus obtained was distilled at 2.3 mm in a column provided with a glass addition of 12 theoretical plates efficiency. Yield: 1) Phenol, 0.8 g, b.p. 48.5°; 2) o-isopropylphenol, 7.0 g, b.p. 61.5°; 3) o-isopropylphenoxyacetic acid, m.p. 130-131° (from water); 4) p-isopropylphenol, 15.2 g, b.p. 74.5°, m.p. 60° (from petroleum ether); 5) p-isopropylphenoxyacetic acid, m.p. 80° (from water). The constants of these substances agree with literature data [4, 5]. The liquid from both Tishchenko flasks was combined, the oily layer separated, washed with a solution of potash and water, dried with anhydrous magnesium sulfate, and distilled. This yielded 5.6 g of 1,2-dibromopropane, b.p. 142-145°, n_D^{20} 1.9254, which agrees with literature data [6].

The alkylations with diphenylbutyl-, isobutyl-, and isoamyl borates, done analogously. For the preparation of diphenylisoamyl borate, the amyl alcohol from fermentation, b.p. 129-132°, was used. sec-Butylphenols were distilled in a column of 12 theoretical plates efficiency. tert-Butylphenols and amyphenols are easily separated on vacuum distillation in a Widmer spiral 12 cm high. The results are given in the table. In all experiments the quantity of phenol was 94 g; KU-2, 5 g.

Conditions and Results of Alkylphenols Synthesis

Alcohol	Alkylation conditions		Refluxed phenol		Alkyl	Characteristics of alkylphenols						Literature
	Time hr.	Temp.	in g	in gram-mole		Yield (g)	Yield, % per phenol char-acted	B.p. (pressure in mm)	M.p.	Alkylphenol, m.p.	Other characteristics of the product	
Propyl	4.5	177—185°	66.0	0.7	{ o-Isopropyl p-Isopropyl	7.0	10.4	61.5° (2.3)	—	130°	—	[4] [5]
						15.2	22.4	74.5 (2.3)	60°	80	—	
Isobutyl	7.5	185—240	50.0	0.532	{ o-sec-Butyl p-sec-Butyl Dibutyl	11.2	24	73.5 (3)	—	112	n_D^{20} 1.5228, d_4^{20} 0.9981, M_{RD} 46.34; calc. 46.42	[7, 8]
						22.0	47.2	84.5 (3)	57.5	—	Soluble in an alcoholic alkali of Kleisen [9] and Cohen [10].	
Isobutyl	4.5	195—240	67.7	0.72	{ p-tert-Butyl ditert-Butyl	33.1	44	149—151 (50)	98 (from H ₂ O)	85—86	—	[10]
						9	8.8	155—167 (50)	—	—	n_D^{20} 1.5126. Soluble in alcoholic alkali of Kleisen [9] and Cohen [10]	
Isoamyl	3.5	182—200	18.4	0.18	{ Mixture of amyl-phenols p-tert-Amyl	8.8	2.7	131—140 (50)	—	—	Soluble in 10% NaOH	[11, 12]
						93.7	30.9	161—165 (50)	91.5 (from petroleum ether)	—	Benzoate, m.p.: 59-60° (from alcohol).	

SUMMARY

It was shown, that when alkylphenyl esters of boric acid are heated in the presence of a strong cationite, a rearrangement of alkylphenyl borates takes place; alkylphenols are obtained by hydrolysis of the rearrangement products.

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SYNTHESIS AND STUDY OF ORGANOSTANNOXANES. I

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Organic tin compounds are used as stabilizers for halogen containing polymeric materials, and also for the synthesis of polymers (on the basis of organotin esters of unsaturated acids [1, 2]).

Starting with the position of tin in the periodic chart of elements, where its immediate analogs are silicon and

germanium which are able in many instances to form polymeric chains of the type $\dots - \overset{\text{Me}}{\underset{|}{\text{O}}} - \overset{\text{Me}}{\underset{|}{\text{O}}} - \dots$

similar compounds can be expected with a tin atom in a macromolecular chain. Such polymers were obtained in the present work (polyorganostannoxanes, polyorganotin silicones, and others), but the molecular weight of the polymers was small (no more than 2000 in a number of cases) [3-7]. The best polymerization stage for polyorganostannoxanes (about 10) was reached when dibutyltin acetate was treated in vacuo by humid air for a comparatively long time [8].

The present work was undertaken in order to study possible syntheses of polyorganostannoxanes based on some dialkyltin dichlorides of the general formula R_2SnCl_2 , where $R = C_2H_5$ and C_3H_7 .

The initial products were prepared by the method proposed by Kocheshkov [9]. Diethyltin dichloride and di-n-propyltin dichloride are white, crystalline compounds, which dissolve in water. When heated in aqueous solution, gradual hydrolysis occurs and infusible and insoluble dialkyltin oxides form.

We prepared alkyltin acetates in an aqueous medium by the action of acetic acid salts on the corresponding dialkyltin dihalides. As was to be expected, we obtained instead of the dialkyltin acetates the products of their hy-

drolysis and condensation, i.e., compounds of the type $CH_3COO \left[\begin{array}{c} R \\ | \\ SnO \\ | \\ R \end{array} \right]_n \begin{array}{c} R \\ | \\ SnOCOCH_3 \\ | \\ R \end{array}$, where $n = 2-3$. The fol-

lowing schemes represent their formation processes:

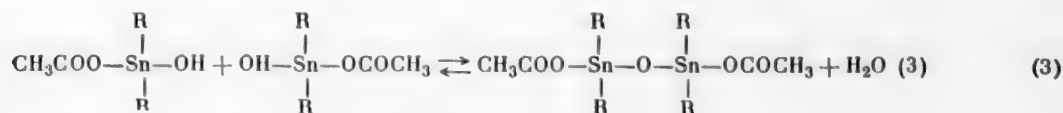
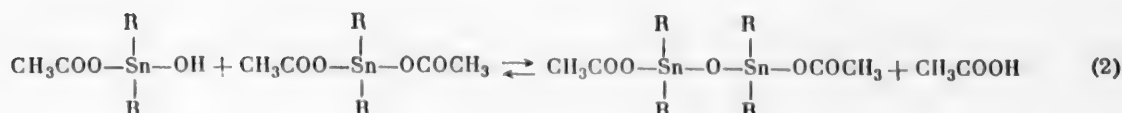
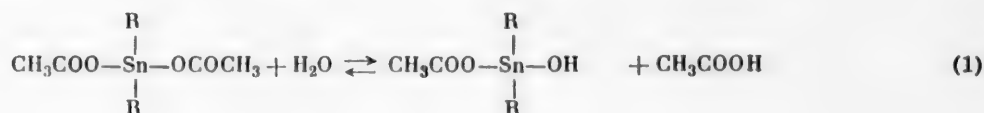


TABLE 1

Compounds	M	Acetate groups, %	Content, %			
			Sn	C	H	O
Polyethylstannoxane acetate	796	14.6	52.64	26.41	4.92	16.03
Hexaethyltristannoxane acetate	681	17.34	52.4	28.6	5.29	14.2
Octaethyltetrastannoxane acetate	874	13.51	54.4	27.5	5.27	12.83
Polypropylstannoxane acetate	898	11.70	—	—	—	—

The reactions were conducted at 0, 20, and 50°. In the synthesis of polyethylstannoxane acetates the substances obtained at 50° did not fully dissolve in benzene due to the presence of diethyltin oxide as an impurity, but the yield was maximum. Compounds obtained at 0 and 20° were very soluble in organic solvents and were similar in molecular weight (714 and 782); but the yield was almost 2.5 times greater when the reaction was conducted at 20°. At that temperature polyethylstannoxane acetates were also obtained. The ratio of the components was equimolecular. In order to prevent the formation of diethyltin oxide, we added about 5% by weight of acetic acid to the solution of sodium acetate, to maintain a pH < 7. The best temperature for the synthesis of polypropylstannoxane acetates turned out to be 50°. There the product obtained was soluble in benzene and other organic solvents. The yield was about 70%. The results of the study of polyorganostannoxanes obtained by us are given in Table 1; for the sake of comparison, specific characteristics of individual compounds are included.

The molecular weight given in Table 1 should be regarded as average, since the products are mixtures of polymeric homologs, as brought out by the interval in their fusibility. Further conversions of these compounds were studied by us. The possibility of increasing the molecular weight of polyalkylstannoxane acetates by their treatment in vacuo with humid air and at different temperatures was studied. The nature of the conversion taking place here can be imagined by the schemes of reactions (1), (2), and (3) given above. The heating and vacuum promote the removal of acid and water formed, but all the time water is being added to the reaction from air through a capillary (the air is first passed through a water layer at 85-90°). The arrangement is equipped with a vacuum trap placed in a Dewar flask with liquid air to collect the acetic acid and water. The residual pressure 5-6 mm. Time of process 3-32 hours. The products were solid and waxy substances, from white to gray in color (depending on the time and temperature of the treatment). With a few exceptions, they give a slightly turbid solution or even a precipitate when dissolved in organic solvents. An increase in the reaction temperature somewhat increases the molecular weight of the soluble portion of the products, but their solubility greatly decreases. The same changes take place with alkylstannoxane acetates when the time of their treatment with humid air in vacuo is increased.

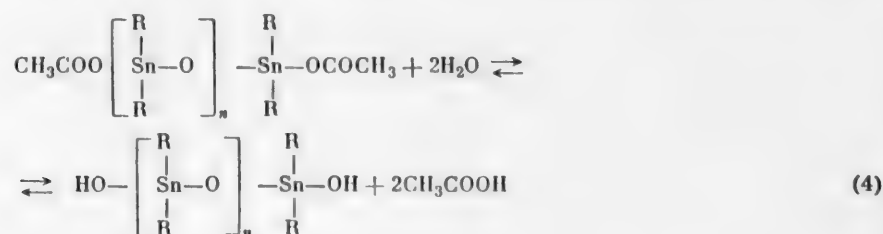
Table 2 gives the dependency of some properties of the products on the reaction conditions.

We did not succeed in increasing the molecular weight significantly by the method described above; the solubility of the polymer became worse. The following elementary analysis was obtained for the insoluble (in benzene and other organic solvents) portion obtained on vacuum treatment of polyethylstannoxane acetate at 180-185° for 6 hours: 60.38% Sn, 15.36% C, 3.03% H, 21.23% O. Comparing these data with the elementary composition of the nucleus of polyethylstannoxane chains $-\text{Sn}(\text{C}_2\text{H}_5)_2-\text{O}$ (61.7% Sn, 24.9% C, 5.18% H, 8.28% O), one can see that the percentage content of oxygen increased at the expense of (a decrease) the content of carbon and hydrogen. One can assume, that separate chains of molecules are connected with one another by oxygen atoms, replacing the ethyl radicals. This replacement evidently takes place in the following manner: The organic radicals linked with a tin atom are capable by the action of organic acids and under certain conditions [11, 12] of being substituted by acid radicals with the formation of the corresponding hydrocarbons. The acetic acid formed as a result of the condensation promotes the cleavage of the alkyl radicals with the formation of acetate groups in the side chain of polymeric molecules. At the point of these acetate groups occurs a "sewing together" of molecules, resulting in difficultly soluble or insoluble compounds. The given method gave no considerable increase in the molecular weight because the water introduced into the reaction zone effected hydrolysis of the polymers, which became stronger with increased temperature and process time.

TABLE 2

Initial compounds	Reaction temperature	Reaction time (in hours)	Solubility in benzene	M
Polyethylstannoxane acetate (mo. wt. 796)	135-140	3	Complete	812
		6		884
		12		908
Polyethylstannoxane acetate (mol. wt. 796)	155-160	3.5	Turbidity on solution	762
		7		803
		12		1028
Polyethylstannoxane acetate (mol. wt. 796)	180-185	2	Much turbidity	—
		4	Precipitate	—
		6	Same	—
Polypropylstannoxane acetate (mol. wt. 898)	135-140	3.5	Complete	1060
		7		1132
		12		1169
		19		1271
Polypropylstannoxane acetate (mol. wt. 898)	155-160	20	Turbidity on solution	1147
		32		1169

When the initial as well as synthesized alkylstannoxane acetates were heated with aqueous solutions of alkalis, more extensive conversions took place than the expected saponification of terminal acetate groups, and products which did not dissolve in organic solvents were formed. Because of the relative hydrolytic instability of the ester bond [10] the cleavage of acetate groups happened on prolonged heating of polyalkylstannoxane acetates with a large excess of water.



The shift in the equilibrium of this reaction was accomplished by the excess of water, and repeated replacement of the solution above the precipitate with distilled water. The acetic acid was titrated with an alkaline solution. The saponification products, i.e., dihydroxyalkylstannoxanes, are white, brittle substances, which pulverize. They start to melt at 200°, and at once again solidify; they are difficultly soluble in benzene and dioxane on heating. The molecular weight of the soluble portion is between 900 and 1000. Without doubt the presence of two terminal hydroxyl groups in compounds of this type is interesting from the view point of their possible polycondensation with suitable di- and polyfunctional compounds (to obtain polymeric materials).

We used the dihydroxypolyalkylstannoxanes for condensation with polyalkylstannoxane acetates. The reaction was conducted in a flask equipped with a Dean and Stark trap at 160-200° at various time intervals. The reaction mass strongly thickened and in the end was a soft, slightly brown, clear mass, which hardly dissolved in organic solvents and somewhat softened at 250°. Such behavior of the resinous substances obtained indicates the presence of a steric structure of the polymer molecules. It is obvious, that in order to get soluble products one must conduct the condensation in a manner where the acetic acid formed is removed as fast as possible from the reaction medium.

EXPERIMENTAL

Synthesis of polyethylstannoxane acetates. Concentrated aqueous solutions of 50 g diethyltin dichloride and 56.8 g sodium acetate to which 1.75 g acetic acid had been added, were combined under stirring at 20° and main-

TABLE 3

Compound	Content of hydroxyl group, %		M	Content			
	Verley	Chugaev-Zerevitinov		Sn	C	H	O
Dihydroxypolyethylstannoxane	4.38	3.54	930	60.06	24.45	4.59	11.00
1,4-Dihydroxyoctaethyltetra-stannoxane	4.30	4.30	790	60.3	24.3	5.32	10.08
1,5-Dihydroxydecaethylpentastannoxane	3.76	3.76	983	60.51	24.4	5.29	9.80
Dihydroxypolypropylstannoxane	—	—	1163	—	—	—	—

tained under those conditions for 1.5 hours. Then the precipitate was filtered, washed with distilled water, and dried first in air, then in a vacuum cabinet at temperatures not exceeding 50°. Yield: 54-55%. Molecular weight (cryoscopically in benzene solution) 700-720. Elementary composition: 52.64% Sn, 26.41% C, 4.10% H.

Synthesis of polypropylstannoxane acetates. To a concentrated aqueous solution of 21.3 g sodium acetate was added at 50° a solution of 20.7 g dipropyltin dichloride in methanol. At the given temperature the mixture was agitated for 1.5 hours, then the filtrate precipitated, washed with distilled water, and dried. Yield: 17.6 g (70.5%). Molecular weight: 883-914.

Synthesis of dihydroxypolyethylstannoxane. To an exactly weighed portion of polyethylstannoxane acetate (no more than 10 g) placed in a flask with a reflux condenser was added 500 ml distilled water and the mixture was heated while boiling for five hours. Then the liquid was decanted and to check the completeness of saponification, titrated with a 0.5 N alkali solution in the presence of phenolphthalein. The residue was again treated with 500 ml distilled water and again boiled for five hours. This operation was repeated several times. The yield was no more than 60%.

Some properties of dihydroxyalkylstannoxanes prepared by us are given in Table 3; for the sake of comparison, specific properties of individual products are also given.

Condensation of polyethylstannoxane acetates with dihydroxypolyethylstannoxanes. The given products were charged in a molecular ratio of 1 : 1 into a flask provided with an agitator and a trap for side products of the reaction. The first three hours the temperature was maintained at 160°, then at 200° for the next five hours. After completion of the reaction some drops of an acid liquid were found in the trap. The product obtained was a sticky, transparent, light brown substance. Yield: 8.9 g (about 80%).

SUMMARY

1. When a reaction was conducted between dialkyltin dichlorides and sodium acetate in an aqueous solution, no monomeric dialkyltin acetates were obtained, but products of their hydrolysis and condensation, namely, polyalkylstannoxane acetates with a degree of condensation $n = 3-4$. When they were heated with water, the corresponding dihydroxyalkylstannoxanes with a fixed content of hydroxyl groups were obtained.
2. When polyalkylstannoxane acetates (alkyl, ethyl, propyl) were treated with humid air in vacuo at various temperatures, no significant increase in the molecular weight of the given compounds was attained.
3. When polyalkylstannoxane acetates were condensed with dihydroxypolyalkylstannoxanes, the resulting products were resinous substances insoluble in usual organic solvents.

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INTRAMOLECULAR CONVERSIONS OF N-ACYL DERIVATIVES OF α, γ -DIAMINO BUTYRIC ACID

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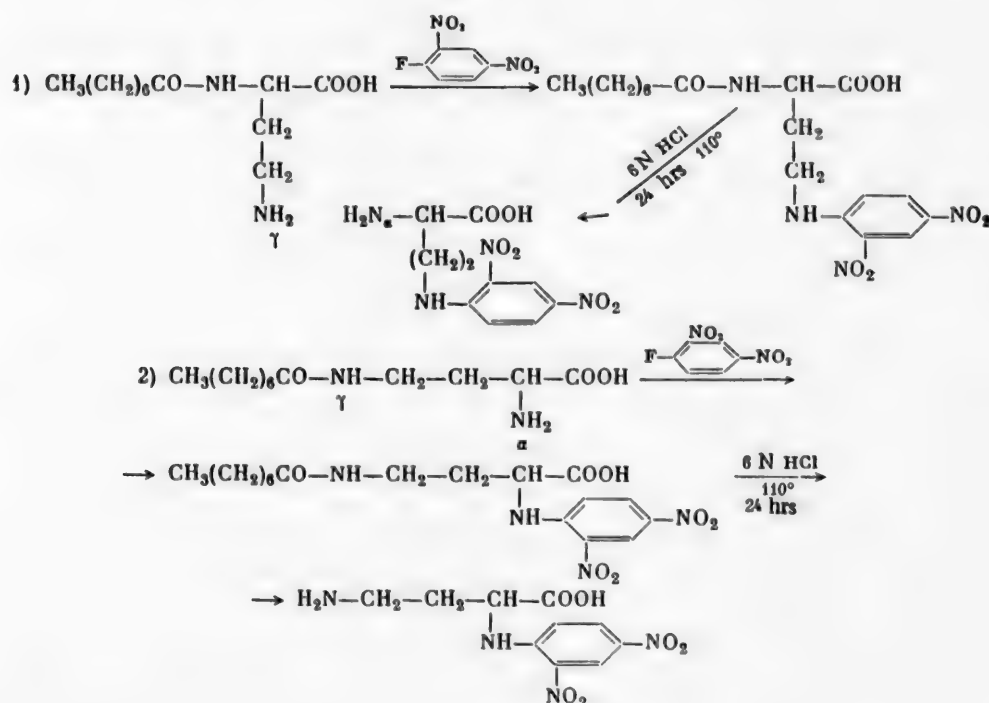
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As shown in a previous communication [1], it was discovered in the Albumin and Antibiotics Laboratory of the chemical faculty of Moscow State University that when polymyxin M is kept thermostatically in a 0.1 N ammonia solution for 3.5 days at 37°, the antibiotic is almost completely inactivated. We showed, that under those conditions a type of isomerization not described in the literature takes place in the peptides of α, γ -diaminobutyric acid, namely migration of the acyl radical from the α - to the γ -amino group of α, γ -diaminobutyric acid ($N^\alpha \rightarrow N^\gamma$ migration).

In order to prove this migration, we selected for the synthetic model α -caprylyl- α, γ -diaminobutyric acid, which with 0.1 N ammonia preserved the activity lost under those same conditions by polymyxin M. The resulting mixture of substances (mixture X) was studied electrophoretically in several electrolytes. The mixture X divided into two substances with almost identical intensity of spots, corresponding to α -caprylyl- and γ -caprylyl- α, γ -diaminobutyric acids (see Figure 1). In addition, electrophoresis in an electrolyte of pH 3 disclosed a spot which was intermediate between α -caprylyl- and γ -caprylyl- α, γ -diaminobutyric acid, and which consequently was of intermediate basicity (Figures 1 and 2).

To demonstrate the conversions described above more graphically caprylyl derivatives of diaminobutyric acid and mixture X, were fully dinitrophenylated and hydrolyzed by 6 N hydrochloric acid at 110° over a period of 24 hours.



The hydrolysis products were studied electrophoretically in a copper acetate buffer. In the hydrolyzate of mixture X we found α -DNP- as well as γ -DNP- α, γ -diaminobutyric acid (see Figure 2).

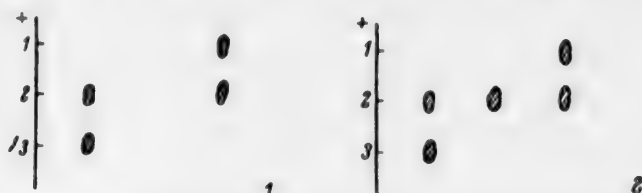


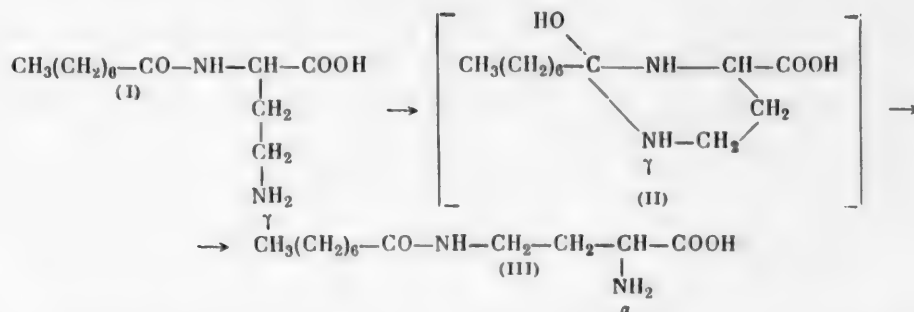
Fig. 1. α -Caprylyl- α, γ -diaminobutyric acid; 2) mixture X; 3) γ -caprylyl- α, γ -diaminobutyric acid. Explanation in text.

From the given data it follows, that mixture X consists of α - and γ -isomers of α, γ -diaminobutyric acid.

It was interesting to find out whether the reverse phenomenon of $N^\gamma \rightarrow N^\alpha$ migration takes place in an acid medium. For this purpose we treated γ -caprylyl- α, γ -diaminobutyric acid thermostatically at 37° with 6 N hydrochloric acid over a period of 3.5 days. Then the mixture thus obtained (mixture Y) was studied electrophoretically, it was found that the mixture consisted of α -caprylyl- and γ -caprylyl- α, γ -diaminobutyric acid, free α, γ -diaminobutyric acid, and of a substance which we did not identify and which moved before α -caprylyl- α, γ -diaminobutyric acid (see Figure 3).

Under the conditions shown above, evidently, partial conversion of the γ -isomer to the α -isomer, i.e., $N^\gamma \rightarrow N^\alpha$ migration, takes place.

It follows from experimental data, that mixture X obtained when α -caprylyl- α, γ -diaminobutyric acid was preserved under conditions where polymyxin M becomes inactive (basic medium) contains, together with α -caprylyl- α, γ -diaminobutyric acid, also γ -caprylyl- α, α -diaminobutyric acid. Evidently the acyl residue of the caprylic acid migrates from the α - to the γ -amino group of α, γ -diaminobutyric acid ($N^\alpha \rightarrow N^\gamma$ migration), which process can be represented by the following equations.



We think that a similar process can proceed via the intermediate (II), which is of intermediate basicity. To this evidently belong the spots which on the electrophoresis diagram are between α -caprylyl- and γ -caprylyl- α, γ -diaminobutyric acid (see Figure 1, 1).

It is characteristic, that when γ -caprylyl- α, γ -diaminobutyric acid is preserved in acid medium, the electrophoresis diagram shows spots which correspond to γ -caprylyl- α, γ -diaminobutyric acid, the α -isomer, and the free acid. This indicates, that under selected conditions the reverse migration of the acyl radical from caprylic acid, $-N^\gamma \rightarrow N^\alpha$, takes place.

The conversions described above, taking place under rather mild conditions, testify to the instability of the amide bond, and also of the peptide bond in peptides of α, γ -diaminobutyric acid.

EXPERIMENTAL

Synthesis of mixture X. Synthetic α -caprylyl- α , γ -diaminobutyric acid (40 mg) was dissolved in 5 ml 0.1 N ammonia and kept thermostatically at 37° over a period of 3.5 days. Then the mixture was several times vacuum steam distilled, the residue was dissolved in 4 ml aqueous ethanol, and the resulting solution was studied electrophoretically (see Figure 1).

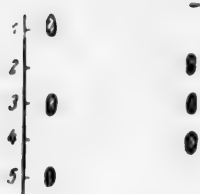


Fig. 2. 1) α -DNP- α , γ -diaminobutyric acid; 2) γ -DNP- α , γ -diaminobutyric acid; 3) complete hydrolyzate of DNP-mixture X; 4) complete hydrolyzate of α -caprylyl- γ -DNP- α , γ -diaminobutyric acid; 5) complete hydrolyzate of γ -caprylyl- α -DNP- α , γ -diaminobutyric acid. 20 V/cm, 4 hours.

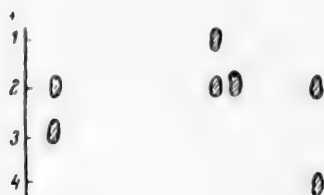


Fig. 3. 1) α -Caprylyl- α , γ -diaminobutyric acid; 2) mixture Y; 3) γ -caprylyl- α , γ -diaminobutyric acid; 4) α , γ -diaminobutyric acid. Electrolyte: 1 N CH_3COOH ; 20 V/cm, 2 hours.

Complete dinitrophenylation on paper. The solution of mixture X obtained as described above was placed on paper strips 12 · 20 cm, 5 cm from the end, 6 μ l at each point, and this was treated under heating in a stream of warm air with a water-alcohol solution of 2,4-dinitrofluorobenzene of 30 mg/ml concentration. The paper strips were kept for three hours in a trimethylamine atmosphere. The trimethylamine was removed with a stream of air. The side products of dinitrophenylation were washed out with benzene, and a saturated 1% solution of acetic acid (1 : 1). The DNP derivatives of mixture X were eluted from the paper with glacial acetic acid. The γ -caprylyl- and γ -caprylyl- α , γ -diaminobutyric acids were dinitrophenylated in an analogous manner.

Complete hydrolysis of DNP derivatives [2]. Hydrolysis of eluted substances from paper was done in sealed ampules in a mixture of equal volumes of glacial acetic acid and concentrated hydrochloric acid at 110° over a 24 hour period. The hydrolyzates were vacuum distilled, dissolved in aqueous acetone, and used for electrophoretic study.

Synthesis of mixture Y. γ -Caprylyl- α , γ -diaminobutyric acid (40 mg) was dissolved in 5 ml 6 N hydrochloric acid and kept thermostatically at 37° for 3.5 days. The resulting mixture was several times vacuum steam distilled, the residue dissolved in aqueous ethanol, and studied electrophoretically.

Conditions of electrophoresis. The electrophoresis was done in an apparatus constructed in the laboratory of albumin and antibiotics chemistry. It operates on the principle of the wet Durrum camera [3]. We used the chromatographic paper of the Leningrad Volodarski works (1958). For the electrophoresis we used strips 34 · 10 cm. The solutions to be studied were placed on the paper strips one cm from the middle line, 4-6 μ l at each point. As a source of supply we used a high voltage VVS-1 rectifier. Benzidine was used to develop the electrophoresis diagram with the N-acyl derivatives of α , γ -diaminobutyric acid.

The following electrolytes were used for electrophoresis of mixtures X and Y: 1) 1 N acetic acid; 2) buffer of pH 2.8: acetic acid-85% formic acid-water (15 : 10 : 2985); 3) buffer of pH 3.0: 2.6 ml 85% formic acid, diluted to 1 liter with water and brought to pH 3.0 by addition of pyridine.

For the electrophoresis of DNP derivatives of α , γ -diaminobutyric acid we used copper-acetate buffer: 2 ml acetic acid-0.6 ml pyridine-497.4 ml water-0.5 g copper acetate.

SUMMARY

1. We discovered a type of isomerization, not described in the literature, of N-acyl derivatives of α , γ -diaminobutyric acid, i.e., $N^\alpha \rightarrow N^\gamma$ migration.

2. It was shown that in acid medium the reverse process $N^\gamma \rightarrow N^\alpha$ migration, takes place.

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THE EFFECT OF IONIZING RADIATION ON CARBOHYDRATES

I. THE PROBLEM OF FORMALDEHYDE AND 1,3-DIHYDROXYACETONE

FORMATION DURING GAMMA-RAY IRRADIATION OF AQUEOUS GLUCOSE, FRUCTOSE, AND MALTOSE SOLUTIONS

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In recent years an intensive study has been made of the action of ionizing radiation on aqueous solutions of mono-, di-, and polysaccharides [1-4]. The authors' attention has centered mainly on the study of highly diluted aqueous solutions (concentration from 0.01 to 0.1 M), for which it has been correctly assumed that the basic action of irradiation is directed to the water molecules; direct activation of the molecule of the irradiated object can be disregarded. Under these conditions water molecules are decomposed into atomic hydrogen and OH radicals. The reaction products of the water "oxols" with the subject being studied and with themselves appear to be the only products resulting. For concentrated solutions the latter proposition is not necessarily correct. As shown by a series of investigators [5, 6], on radiolysis of concentrated aqueous salt solutions considerable change in product yield takes place (calculated per 100 ev), depending on the concentration, this, in the authors' opinion, being an indication of the excitation of the salt molecules under investigation themselves.

Radiolysis products of dilute aqueous glucose solutions have been studied in sufficient detail by Khenokh [1] and by Phillips and co-workers [2]. The authors have indicated that formation of d-glucuronic, d-gluconic, saccharic acids, formaldehyde, glyoxal, 1,3-dihydroxyacetone, d-arabinose, and d-erythrose takes place.

We were interested in studying in more detail yields of the destruction products of the destruction of the monose C - C bond, namely, those of formaldehyde and 1,3-dihydroxyacetone.

EXPERIMENTAL

As the basic products for investigation we chose glucose, fructose, and maltose. Glucose and fructose solutions of concentrations 10, 20, and 30% were prepared in twice-distilled water, poured into ampoules in a stream of nitrogen, sealed, and sterilized at 80° for 1 hour. The solutions were irradiated with Co⁶⁰ gamma-rays. Intensity of the dose was 36.6 roentgens/sec. The maximum total dose applied was 46.10⁶ roentgens.

Formaldehyde was determined by the method described in [7]. To characterize the change in amount of dihydroxyacetone, the change in optical density of the absorption maximum occurring at λ 263 m μ was used. This maximum is attributed to dihydroxyacetone formation. Solutions irradiated with a definite dose were diluted 100 times with distilled water and optical density of the solution at λ 263 m μ measured on an SF-4 spectrophotometer. Cell thickness was 1 cm. It had first been demonstrated that under the conditions of the experiment the position of maximum absorption does not change with change in irradiation dose.

Results Obtained and Discussion

Calculations of the effective atomic numbers [8] for the aqueous glucose and fructose solutions at the concentrations used showed that the proportion of the total amount of energy absorbed by the carbohydrate molecules was 9-25% of the total energy absorbed. On changing solution concentrations from 10 to 20 and 30%, the ratio of the energies necessary per carbohydrate molecule changes to 0.65 : 1.2 : 1.8, while for water this energy ratio is equal to 6.5 : 5.9 : 5.3 respectively. By increasing concentration of glucose, fructose, and maltose the energy absorbed by the subjects studied themselves increased almost three times, but the energy absorbed by the water fell only slightly (on changing the concentration from 10 to 30% by a total of 20%). In the event of the possibility of formation of certain products by direct excitation of the carbohydrate molecule, such increase in the energy absorbed by them cannot affect total yield of the product.

Change in Optical Density at λ 263 m μ for Irradiated Glucose, Fructose, and Maltose Solutions of Various Concentrations

Dose of irradiation (roentgen)	Optical density of solutions								
	glucose concentration (in %)			maltose concentration (in %)			fructose concentration (in %)		
	10	20	30	10	20	30	10	20	30
4.2 · 10 ⁶	—	—	—	—	—	—	0.11	0.1	0.11
9	0.085	0.070	0.075	0.050	0.056	0.051	—	—	—
11	—	—	—	—	—	—	0.32	0.25	0.31
15	—	—	—	—	—	—	0.40	0.37	—
18	0.21	0.22	0.21	0.16	0.16	—	—	—	—
28	0.34	0.34	0.31	—	—	—	—	—	—
37	0.53	0.51	0.45	0.28	0.28	0.26	—	—	—
46	0.62	0.61	0.51	—	—	—	—	—	—
50	—	—	—	0.36	0.38	0.36	—	—	—

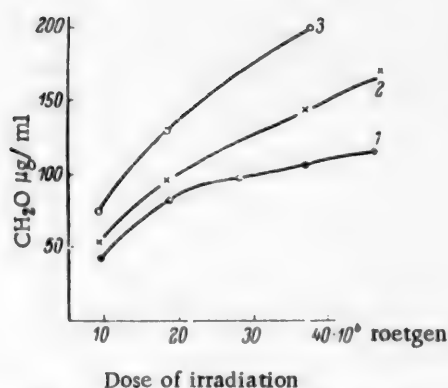


Fig. 1. Yield of formaldehyde, depending on dose of irradiation of aqueous glucose solutions of various concentrations. 1) 10%; 2) 20%; 3) 30%.

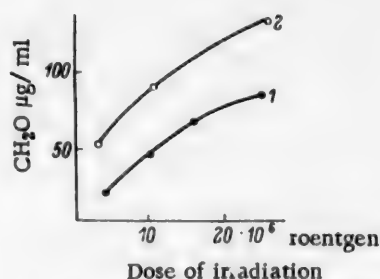


Fig. 2. Yield of formaldehyde, depending on dose of irradiation of aqueous fructose solutions of various concentrations. 1) 10%; 2) 20%.

Results of experiments to study formaldehyde yield resulting from irradiation of aqueous glucose and fructose solutions are shown in Figs. 1 and 2.

As seen from the results given, with increase in the original concentration of the carbohydrates studied, a considerable increase in formaldehyde yield is observed. Yield of the latter for glucose at an irradiation dose of $9 \cdot 10^6$ roentgens increases from 1.8 to 2.2 and 3.1 moles per 100 ev on changing concentration from 10 to 20 and 30% respectively.

To characterize the change in amount of 1,3-dihydroxyacetone the change in optical density at wavelength 263 m μ was used [2]. As seen from the results of the experiments (see Fig. 3), within the limits of irradiation dosage change $9 \cdot 10^6$ to $46 \cdot 10^6$ roentgens, increase in optical density varies linearly with increase in dosage. In the table are shown values of optical density (D) for glucose, fructose, and maltose solutions of various concentrations.

As seen from the results given, the value of the optical density on irradiating a solution with one and the same dose does not depend, with the limits of measurement error, on carbohydrate concentration used. Thus, at dosage $9 \cdot 10^6$ roentgens, optical density of a glucose solution amounts to 0.085, 0.075, and 0.075 for concentrations 10, 20 and 30% respectively, and at dosage $18 \cdot 10^6$ roentgens — 0.21, 0.22, 0.21; for maltose, 0.056 and 0.051 for concentrations 20 and 30% (dosage $9 \cdot 10^6$ roentgens), etc.

Independence of yield of 1,3-dihydroxyacetone on carbohydrate concentration can occur only if the former is formed as a result of destruction of the carbohydrate molecule by water radicals. Yield of these initial radiolysis products would not be changed to any great extent under the experimental conditions, since the amount of energy absorbed by the water molecules falls only slightly. In the case of large excess of carbohydrate, the reaction rate

of the system would be determined only by the rate of formation of reacting radicals. If formation of a product by direct excitation of the molecule studied and its subsequent destruction were possible, increase in yield of this product would be observed with increase in carbohydrate concentration taking place during formaldehyde formation.

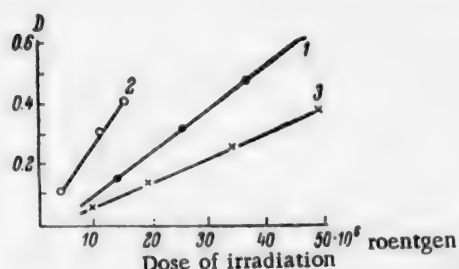


Fig. 3. Relation between optical density (D) λ 263 m μ of glucose (1), fructose (2), and maltose (3) solutions and irradiation dose.

On the basis of the results obtained it could be expected that destruction at the third carbon atom in the absence of conditions for formation of mobile free radicals would not be observed at the same time that formaldehyde formation was taking place. The results of irradiating solid glucose are indication of the possibility of the correctness of this assumption. Aqueous solutions of glucose irradiated in the solid state did not show an absorption band with a maximum in the region 260 m μ (Fig. 4), formaldehyde formation being observed, however.

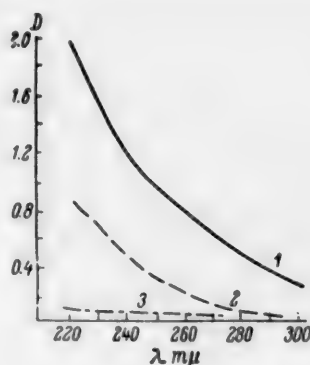


Fig. 4. Spectrum of 0.1-0.3% solutions of glucose irradiated in the dry form with doses: 1) $110 \cdot 10^6$ roentgens; 2) $80 \cdot 10^6$ roentgens; 3) nonirradiated glucose.

SUMMARY

1. It was shown that on irradiating aqueous carbohydrate solutions the value of the optical density at maximum absorption changes linearly with increase in irradiation dosage.

Value of optical density does not depend on original carbohydrate concentration within the limits of change in the latter from 10 to 30%.

2. Formaldehyde yield during irradiation increases with increase in concentration of glucose and fructose.

3. The proposal was made that one of the types of destruction during direct excitation of the carbohydrate molecule by gamma-rays leads to formaldehyde formation. Formation of 1,3-dihydroxyacetone also takes place only as a result of destruction by free radicals – by "oxols" of water.

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SUBSTITUTED LACTONES AND THEIR CONVERSIONS

I. CONDENSATION OF γ -HEPTYLBUTYROLACTONE WITH ALDEHYDES AND KETONES

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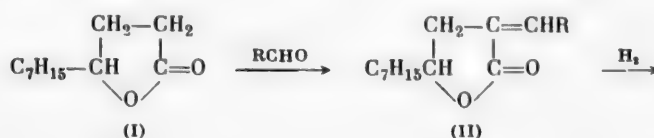
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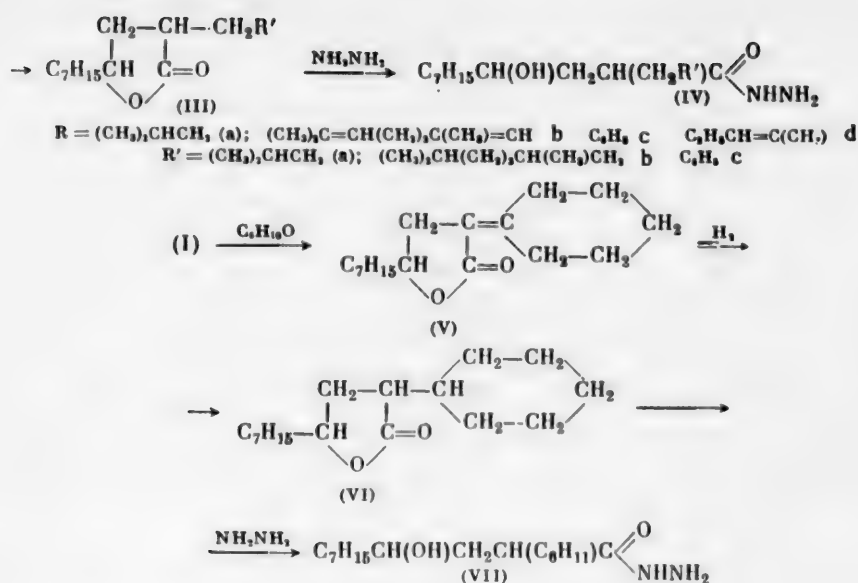
In the literature there are repeated references to the fact that certain α -alkyl-substituted butyrolactones and γ -valerolactones possess odors of interest in perfumery [1]. However, synthesis of these compounds is relatively complex. In the search for a more convenient method of synthesizing these compounds we turned to condensation of butyrolactone and γ -valerolactone with carbonyl compounds, leading to α -alkylidene-substituted lactones, by hydrogenation of which could be obtained α -alkyl-substituted lactones. This reaction has been accomplished in the case of a few aromatic aldehydes by a series of investigators [2-4], and also recently in more detail by Zimmer and Rothe [5], who obtained in this manner a large number of α -arylmethylenebutyrolactones and α -arylmethylbutyrolactones. However, the condensation interest to us, that of lactones with aliphatic and alicyclic carbonyl compounds, was accomplished only in the case of heptanal [2], nonanal, cyclohexone [3], and isovalerianaldehyde [5]. Wishing to ascertain the applicability of this reaction to γ -substituted butyrolactones and extend it to a larger number of aliphatic and alicyclic carbonyl compounds, we investigated the condensation of γ -heptylbutyrolactone (I) (undecalactone) with benzaldehyde, isovalerianaldehyde, citral, cyclohexanone, and 2-methylpenten-2-al. It appeared that γ -heptylbutyrolactone condenses in presence of sodium methylate with the carbonyl compounds mentioned, forming in 35-76% yield α -alkylidene- γ -heptylbutyrolactones previously undescribed: α -benzylidene- γ -heptylbutyrolactone (IIc), α -(3-methylbutylidene)- γ -heptylbutyrolactone (IIa), α -(3,7-dimethyloctadien-2,6-ylidene)- γ -heptylbutyrolactone (IIb), α -cyclohexylidene- γ -heptylbutyrolactone (V). Hydrogenation of these lactones by a method described previously [3] led to the corresponding α -alkyl- γ -heptylbutyrolactones: α -benzyl- γ -heptylbutyrolactone (IIIc), α -(3-methylbutyl)- γ -heptylbutyrolactone (IIIa), α -(3,7-dimethyloctyl)- γ -heptylbutyrolactone (IIIb), α -cyclohexyl- γ -heptylbutyrolactone (VI). Yields and constants of the substances obtained are shown in Table 1.

Both the α -alkylidene- γ -heptylbutyrolactones and their hydrogenation products possess powerful odors, reminiscent of the odor of undecalactone. The saturated lactones obtained were identified by their conversion into the hydrazides of the corresponding hydroxy acids (IV) and (VII) by the action of hydrazine hydrate. The structure of α -benzylidene- γ -heptylbutyrolactone (IIc) is confirmed by formation of benzaldehyde on its oxidation with potassium permanganate. By similar oxidation of α -cyclohexylidene- γ -heptylbutyrolactone (V) cyclohexanone is formed.

The structure of the condensation products, in addition to the above-mentioned conversions, was confirmed by the data of elementary and functional analysis, and also by u.v. -spectral data* indicating the presence in the condensation products of a double bond conjugated with the double bond of the carbonyl group of the lactone ring. In the spectra of α -(3-methylbutylidene)- γ -heptylbutyrolactone (IIa) and α -cyclohexylidene- γ -heptylbutyrolactone (V) a very clearly defined maximum occurs in the region 225-235 m μ , which after hydrogenation of these lactones disappears almost completely. In the u.v. -spectrum of α -benzylidene- γ -heptylbutyrolactone (IIc) there is also a very clearly defined maximum (λ_{\max} 284 m μ), but considerably displaced toward the long-wave region of the spectrum. Exaltation of molecular refraction on conversion from α -alkylidene-substituted lactones to their hydrogenation products also disappears.



*U.v. -spectra taken by R. I. Sharapova.



The structure of α -benzyl- γ -heptylbutyrolactone (IIIc) is confirmed by formation of benzoic acid on oxidation of this lactone with potassium permanganate.

Condensation of 2-methylpenten-2-al with γ -heptylbutyrolactone is accompanied by formation of a substance of unknown structure, close in boiling point to normal reaction product - α -(2-methylpenten-2-ylidene)- γ -heptylbutyrolactone (IIId), and so it was not possible to isolate it from the fraction with b.p. 160-205° at 1.5 mm, n_D^{20} 1.4905, containing, judging by the saponification number, 87% of this lactone.

TABLE 1

Substance no.	Yield (purity in parenthesis) (in %)	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	$M R_s$	
					found	calculated
IIc*	76 (99)	204° (1) M.p. 40.5	1.5400 (40°)	—	—	—
IIa*	44 (96)	163—165 (1.5)	1.4690	0.9235	76.12	75.08
IIb	35 (94)	230—240 (2)	1.5150	0.9559	—	—
Y*	49 (99.5)	192—195 (3)	1.4950	0.9888	77.96	77.50
IIIc	75 (98.5)	184—192 (2)	1.5001	0.9948	81.14	81.10
IIIa	70 (96)	175—185 (10)	1.4537	0.9159	75.13	75.54
IIIb	65 (99)	220—230 (7)	1.4649	0.9125	98.30	98.63
VI	80 (100)	212—213 (12) M.p. 41°	1.4770 (40°)	—	—	—

* λ_{max} (in alcohol): (IIc) 284 m μ (lg ϵ 4.32); (IIa) 225 m μ (lg ϵ 3.97); (V) 235 m μ (lg ϵ 4.06).

On condensing γ -heptylbutyrolactone (I) with cyclohexanone together with α -cyclohexylidene- γ -heptylbutyrolactone (V), acid (VIII) is also formed, which is evidently γ -methoxyundecanoic acid. This acid is formed most rapidly from γ -heptylbutyrolactone (I) and sodium methylate. Similar rupture of the lactone ring under the action of sodium ethylate is known, in particular, for γ -butyrolactone, from which by this route γ -ethoxybutyric acid is formed [6].

With the aim of investigating the possibility of converting the lactones obtained into cyclopentenone derivatives by dehydration in presence of polyphosphoric acid by the method described previously (see review [7]), we

studied the reaction of these lactones with polyphosphoric acid. It appeared that α -alkyl-substituted lactones on heating with polyphosphoric acid to 100-120° are unchanged. At higher temperatures resinification of the substance occurs, unaccompanied by formation in any noticeable amounts of carbonyl compounds.

EXPERIMENTAL

Condensation of γ -Heptylbutyrolactone (I) with Aldehydes and Ketones. In a three-necked flask fitted with stirrer and reflux condenser was placed a mixture of 0.6 mole of γ -heptylbutyrolactone (I) and 0.9 mole of aldehyde or ketone in 400 ml of anhydrous benzene. To this mixture with vigorous stirring was gradually (over 15-30 minutes) added 0.9 mole of powdered sodium methylate, prepared from anhydrous methanol and sodium. The reaction mixture was then usually warmed to 40-50°; if heat evolution was slight, the mixture was warmed up to the temperature indicated. The mixture was stirred for 2.5 hours, left for 16-20 hours, then 250 ml of 20% sulfuric acid added and stirred for 1 hour. The aqueous layer was separated, extracted with benzene, the benzene extracts united with the benzene solution, washed with sodium bicarbonate solution and water, benzene then evaporated off, and the residue distilled in vacuo. To determine the constants and obtain analytical samples the substance was distilled once more. Sample purity was determined by means of the saponification number.

TABLE 2

Substance no.	Molecular formula	Analytical results (in%) (calculated values in parentheses)
(IIc)	C ₁₈ H ₂₄ O ₂	C 79.10, 79.58 (79.37) H 9.18, 9.38 (8.88)
(IIa)	C ₁₆ H ₂₈ O ₂	C 75.83, 75.82 (76.14) H 11.51, 11.26 (11.18)
(V)	C ₁₇ H ₂₈ O ₂	C 76.82, 76.69 (77.22) H 10.90, 10.37 (10.67)
(VIII)*	C ₁₂ H ₂₄ O ₃	C 66.30, 66.45 (66.63) H 11.44, 11.22 (11.18)
(IIIc)	C ₁₈ H ₂₈ O ₂	C 78.93, 78.88 (78.79) H 9.64, 9.87 (9.55)
(IIIb)	C ₁₆ H ₃₀ O ₂	C 75.52, 75.60 (75.53) H 11.98, 12.28 (11.89)
(IIIc)	C ₂₁ H ₄₀ O ₂	C 77.91, 78.10 (77.72) H 12.21, 12.03 (12.42)
(VI)	C ₁₇ H ₃₀ O ₂	C 76.83, 77.14 (76.64) H 11.61, 11.21 (11.35)
(IVc)	C ₁₈ H ₃₀ O ₂ N ₂	N 9.04 (9.14)
(IVa)	C ₁₆ H ₃₄ O ₂ N ₂	N 9.63, 9.84 (9.78)
(IVb)	C ₂₁ H ₂₄ O ₂ N ₂	N 7.73, 7.46 (7.86)
(VII)	C ₁₇ H ₃₄ O ₂ N ₂	N 9.05, 9.29 (9.39)

* Acid number 260; calc. 258.9.

In view of the fact that no success was achieved in isolating substance (IIb) in pure form, its further conversion was carried out without subsequent purification.

On fractional distillation of condensation product (V) from the partially crystallized main fraction with b.p. 170-180° at 2 mm, several grams of substance (VIII) were obtained, m.p. 74° (from isooctane); not investigated more closely.

Analytical results for the substances obtained are shown in Table 2.

Hydrogenation of α -Alkylidene-Substituted Lactones. In a rotary stainless steel autoclave of 150 ml capacity were placed 12-20 ml of α -alkylidene-substituted lactone dissolved in an equal volume of alcohol, and about 1 g of Raney nickel. Hydrogen was forced into the autoclave to 190-200 at., then heated to 100° and the mixture stirred for 1-1.5 hours. On cooling, pressure in the autoclave fell to 160-180 at. The catalyst was filtered off, the filtrate evaporated and the residue distilled in vacuo.

Preparation of Hydrazides of γ -Hydroxy Acids from α -Alkyl- γ -heptylbutyrolactones. A mixture of 1.5 g of lactone and 2 ml of 80% aqueous hydrazine hydrate solution was heated for 1 hour on a water bath. On cooling the mixture solidified to a colorless, crystalline mass. The substance was recrystallized from alcohol 4-5 times.

Melting points of hydrazides: of α -benzyl- γ -hydroxyundecanoic acid (IVc) 142°; α -(3-methylbutyl)- γ -hydroxyundecanoic acid (IVa) 144°; α -(3,7-dimethyloctyl)- γ -hydroxyundecanoic acid (IVb) 132°; and of α -cyclohexyl- γ -hydroxyundecanoic acid (VII) 175°.

Oxidation of Lactones with Potassium Permanganate. 2 g of α -benzylidene- γ -heptylbutyrolactone (IIc) was boiled for 0.5 hour with 0.6 g of caustic soda in 25 ml of water. To the resulting solution of the sodium salt of the hydroxy acid were added 75 ml of water, 45 ml of benzene, and with stirring and cooling with ice 50 ml of saturated potassium permanganate solution gradually added to the mixture. The precipitate of manganese dioxide settling out was separated, washed with benzene, the united benzene extracts evaporated to a small volume and treated with an alcoholic solution of 2,4-dinitrophenylhydrazine sulfate. The precipitate settling out (about 0.5 g) was recrystallized three times from acetic acid, m.p. 237°. According to the data in the literature, the 2,4-dinitrophenylhydrazone of benzaldehyde has m.p. 237° [8]. A sample mixed with an authentic sample gave no melting point depression.

On oxidizing 2 g of α -cyclohexylidene- γ -heptylbutyrolactone (V), carried out in the same manner with subsequent action of 2,4-dinitrophenylhydrazine, 0.4 g of the 2,4-dinitrophenylhydrazone of cyclohexanone was obtained, m.p. 162° (from CH_3COOH), m.p. 162° [8]. A mixed sample gave no melting point depression.

2 g of α -benzyl- γ -heptylbutyrolactone (IIc) was saponified as described above. To the resulting solution of the hydroxy acid salt was added 7 g of potassium permanganate in 150 ml of water and the mixture boiled for 1.5 hours. The manganese dioxide precipitate was separated, washed with water, the filtrate and wash waters made acidic to congo and extracted with benzene. The benzene extracts were evaporated, and the residue distilled in vacuo. The fraction with b.p. 90-110° at 3 mm (0.35 g) crystallized. After drying on a porous plate and recrystallizing from water, m.p. was 122°; for benzoic acid, m.p. 122° [9]. A mixed sample gave no melting point depression.

SUMMARY

1. By reacting γ -heptylbutyrolactone (undecalactone) with aliphatic and alicyclic carbonyl compounds, previously undescribed α -alkylidene- γ -heptylbutyrolactones were synthesized.
2. By hydrogenating α -alkylidene- γ -heptylbutyrolactones, α -alkyl- γ -heptylbutyrolactones were obtained, forming by the action of hydrazine hydrate hydrazides of α -alkyl- γ -hydroxyundecanoic acids.
3. The resulting α -alkyl- γ -heptylbutyrolactones were not converted to alkylcyclopentenones by the action of polyphosphoric acid.
4. The resulting α -alkylidene- γ -heptylbutyrolactones and α -alkyl- γ -heptylbutyrolactones possess obtrusive odors, similar to the odor of undecalactone.

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THE MECHANISM OF THE REACTION OF URIC ACID WITH ACETIC ANHYDRIDE

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On prolonged boiling of uric acid (I) in acetic anhydride, 8-methylxanthine (IX), acetic acid, and carbon dioxide are formed [1]. By observing certain conditions, this reaction can be arrested at the stage where an intermediate compound is formed – the triacetyl derivatives of 4,5-diaminouracil (VI) [2] – or can be directed to formation of the diacetyl derivative of 4,5-diaminouracil [3].

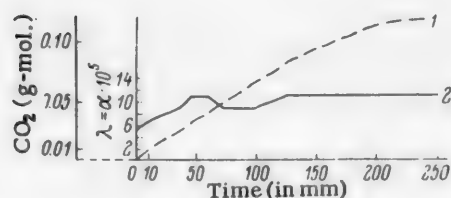
To explain the mechanism of the reaction of uric acid with acetic anhydride a series of schemes have been proposed [2, 4-6]. However, none of these schemes is in accord with experimental data and they consequently do not indicate the reaction mechanism. For instance, Bredereck, Hennig, and Pfeleiderer, proposing a very general scheme for the mechanism of the reaction indicated [2], express the opinion that in the process of formation of the triacetyl derivative of 4,5-diaminouracil a carbon dioxide molecule is first formed, and then an acetic acid molecule. Accordingly, it would be expected that with formation of the intermediate compound indicated the electroconductivity of the reaction mixture would increase correspondingly and would reach a maximum value after cessation of carbon dioxide evolution. All this has not been confirmed by experimental verification. In experiments carried out by us it has been established that in preparation of the triacetyl derivative of 4,5-diaminouracil at the beginning of the process actually noticeable lowering of the ohmic resistance of the reaction mixture is observed. About 40 minutes after beginning the reaction, it reaches a minimum and then remains constant for some time. One hour after beginning the experiment the ohmic resistance of the reaction mixture begins to rise rather rapidly and after a certain period of stabilization again falls. Having reached the level of the first minimum, it remains constant. It should be noted particularly that carbon dioxide evolution in this case ceases much later than final stabilization of the ohmic resistance of the reaction mixture. The data of our experiments is presented in the diagram: on the abscissa axis-time in minutes, and on the ordinate axis-electroconductivity in reciprocal ohms (α), multiplied by 10^5 . Data on carbon dioxide evolution over the corresponding period of time is simultaneously introduced.

As seen from the figure, the electroconductivity curve has two maxima. This permits the proposal that during the reaction acetic acid produced in one of the first stages of the process is reabsorbed by the reaction products and only after a second rupture does its concentration in the reaction mixture become constant. Such an unusual change in electroconductivity of the reaction mixture during preparation of the triacetyl derivative of 4,5-diaminouracil cannot be explained by the schemes proposed. With the aim of elucidating the actual mechanism we have carried out experiments on the isolation of the intermediate products of this reaction and the establishment of their structure.

The first attempts at elucidating the structure of the primary intermediate reaction products formed on reacting uric acid with acetic anhydride were performed by Biltz and Pardon. They came to the conclusion that as the first reaction product in the case under consideration the diacetyl derivative of uric acid is formed [7], and crystallizes as octahedra.

By boiling uric acid for 4.5 hours in 100 times its amount of acetic anhydride, we succeeded in obtaining a substance which crystallized as large, well-formed octahedra. In its physico-chemical properties it was identical with the substance described by Biltz and Pardon. Having in mind the analytical data and certain characteristics of the chemical properties of the substance (see below), we came to the conclusion that the compound obtained was not the diacetyl derivative of uric acid, but was an equimolar mixture of two substances – 7-acetyluric acid (II) and 4-carbacetoxamino-5-diacetylaminouracil (III).

Regarding the substance obtained as an equimolar mixture, all its chemical properties could be readily explained. For instance, on boiling the octahedra in a mixture of acetic anhydride, acetic acid, and pyridine bases i.e., under conditions in which uric acid is converted to 4,5 di(acetylamino)-uracil [3], carbon dioxide was evolved, and the indicated diacetyl derivative of 4,5-diaminouracil was formed. In this connection under normal conditions carbon dioxide was evolved at the rate of 74 ml per 1 g of octahedra, which amounts to about 86% of the theoretical amount. On heating the octahedra obtained with acetic acid in presence of dimethylaniline, carbon dioxide was again evolved, but only to half the extent of that applying on heating with acetic anhydride. In this case as the final reaction products were obtained, besides carbon dioxide, uric acid, 4-amino-5-acetylamino-uracil, and 4,5-di(acetylamino)-uracil. Formation of these products, as seen from the structural formulas of compounds (II) and (III), proceeds as a result of hydrolysis and acidolysis of both components of the equimolar mixture. On boiling with water 1 g of the resulting substance, 42 ml of CO_2 was evolved. Considering that in this case formation of carbon dioxide was possible



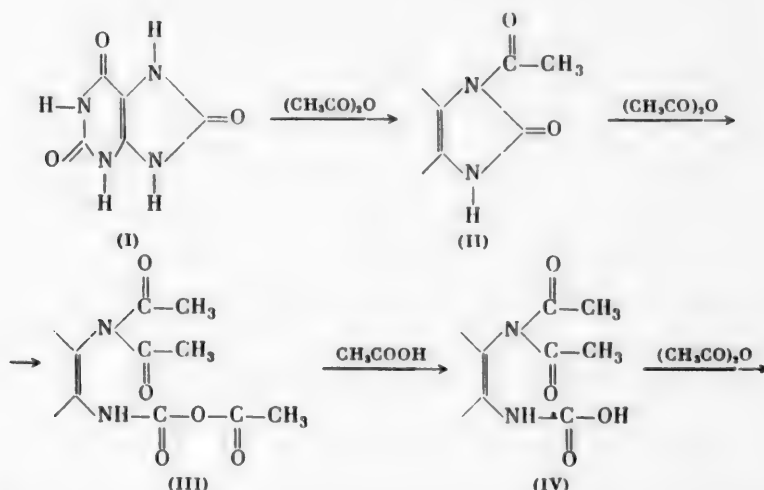
CO_2 evolution (1) and change in electroconductivity (2) during preparation of the triacetyl derivative of 4,5-diaminouracil.

owing to hydrolysis and subsequent decarboxylation of only one component of the mixture (II), the quantity of CO_2 evolved amounted to 97.5%. As a result of hydrolysis of the second component (II) with water, uric acid was formed, obtained from the reaction mixture in 83.5% yield. On reacting the substance obtained under the usual conditions with aniline in absolute ether, acetanilide was formed. In this case the substance appeared to be an anhydride, capable of replacing the hydrogen of the amino group by acetyl. Yield of acetanilide under the conditions indicated amounted to about 1 mole per 1 mole of equimolar mixture.

It is obvious that on methylation of such an equimolar mixture with diazomethane formation would be expected of 1,3,9-trimethyl-7-acetyluric acid as a result of methylation of 7-acetyluric acid (II).

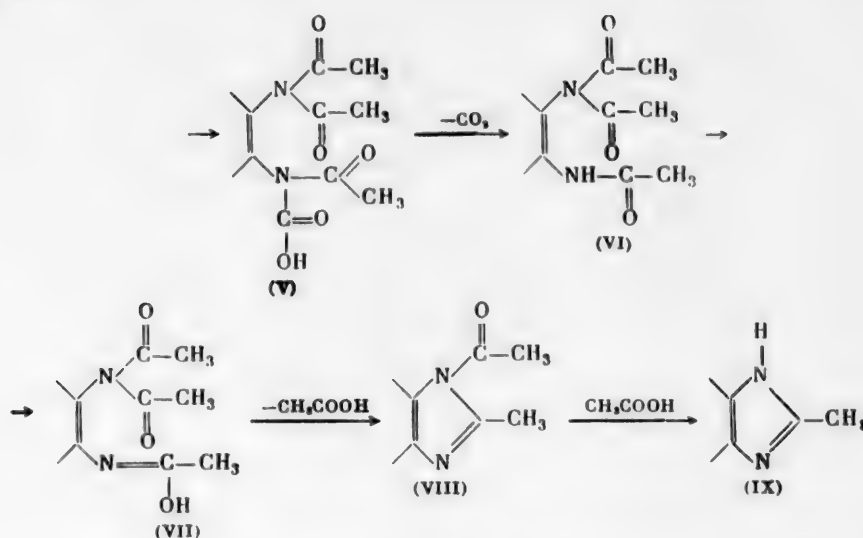
This had also been established experimentally on one occasion by Biltz and Pardon [7].

The data obtained on the structure of the primary intermediate products permitted us to regard in a different light the mechanism of this reaction in the first stages of the process, when uric acid is converted into the triacetyl derivative of 4,5-diaminouracil. Regarding the end of the reaction, i.e., conversion of the indicated triacetyl derivative into 8-methylxanthine, this problem had already been studied sufficiently. In the investigations carried out [8] it was established that the intermediate compound (VI) does not possess a bicyclic structure, as had been proposed until that time [2,5,6], but is 4-acetylamino-5-di(acetylamino)-uracil (VI)*. It has been established experimentally that conversion of compound (VI) into 8-methylxanthine proceeds with formation of intermediate compounds (VII) and (VIII).



* In 1959 additional data was published by E. S. Golovchinskaya [9] confirming our point of view on the structure of the triacetyl derivative of 4,5-diaminouracil.

The above now permits representation of the mechanism of the reaction between uric acid and acetic anhydride by the following scheme:



With the help of the scheme presented, all the features can be explained in the reaction of uric acid with acetic anhydride and corresponding practical conclusions can be made on the possibility of regulating and directing the process. For instance, in particular, accumulation of acetic acid in the reaction mixture during preparation of the triacetyl derivative of 4,5-diaminouracil (VI) from uric acid becomes understandable. In this case, formation of acetic acid takes place during formation of intermediate compounds (II) and (V), and its absorption on acidolysis of compound (III). This also leads to the occurrence of two electroconductivity maxima in the reaction mixture.

In the scheme set out the formation of intermediate compound (V) has been as yet insufficiently substantiated experimentally. Preparation of the triacetyl derivative of 4,5-diaminouracil (VI) can be achieved not only via acetylation of compound (IV) with subsequent decarboxylation of intermediate compound (V) formed, but also via preparatory decarboxylation of compound (IV), with subsequent acetylation of the 4-amino-5-di(acetylamino)-uracil formed. Bearing in mind that in preparation of compound (VI) carbon dioxide evolution still continues after cessation of change in electroconductivity of the reaction mixture (see figure), it is very likely that formation of intermediate compound (V) occurs during the reaction.

EXPERIMENTAL

Acetylation of Uric Acid (I). (a) Preparation of 4-Acetyl-5-diacetylaminouracil (VI) with Simultaneous Measurement of Ohmic Resistance of Reaction Mixture.

Into a 200 ml three-necked flask fitted with stirrer, thermometer, and reflux condenser with platinum electrodes mounted in it*, were introduced 85 ml of acetic anhydride, 34 ml of pyridine bases**, and 16.8 g (0.1 mole) of uric acid. To measure the carbon dioxide evolved during the reaction, the end of the condenser was connected to a gasometer. Ohmic resistance of the reaction mixture was measured by a conductometer connected to the platinum electrodes.

With constant stirring, the contents of the flask were boiled until carbon dioxide evolution ceased, thus usually lasting about 4 hours. After this time about 2650 ml of gas had been evolved. After cessation of carbon dioxide evolution the reaction mixture was cooled to room temperature, filtered, and the precipitate on the filter washed with dry dichloroethane and then with absolute ether. Yield of dry unpurified 4-acetyl-5-diacetylaminouracil was 20.5 g.

Isolation of the resulting triacetyl derivative of 4,5-diaminouracil in the pure state and its conversion into the diacetyl derivative of 4,5-diaminouracil were carried out in the manner described previously [8].

* The stirrer with mercury seal, reflux condenser, and thermometer were mounted on ground-glass fittings.

** The pyridine bases (b.p. 125-135°C) used were anhydrous.

(b) Preparation of Equimolar Mixture of 7-Acetyaluric Acid (II) and 4-Carbacetoxiamino-5-diacetylaminouracil

(III).

Into a round-bottomed 1000 ml flask fitted with reflux condenser were introduced 700 ml of acetic anhydride and 7 g of well-ground uric acid. The top end of the condenser was sealed with a calcium chloride tube. The mixture was boiled for 4.5 hours. The contents of the flask were then cooled to 70-80°C and filtered from the precipitate of undissolved uric acid. The filtrate was transferred to a flask sealed with a calcium chloride tube, and left to stand at room temperature for 15-20 hours. From the filtrate a precipitate of octahedra settled out with a trace of a small amount of a substance crystallizing as small, fine needles. Yield of the precipitate, washed on a filter with dichloroethane and then dried over caustic soda, amounted to 3.5-3.8 g. The filtrate obtained after separation of this precipitate was concentrated in vacuo at 45-50° to a volume of 100 ml. After cooling and filtering, an additional 1.4-1.6 g of the product was obtained. Total yield of unpurified product was 5.1-5.2 g.

The crystalline mixture obtained was dissolved with heating in 100 times its amount of acetic anhydride and left to crystallize at room temperature for 15-20 hours. The precipitate settling out was filtered off, washed and dried as indicated above. Yield of pure octahedra was 3 g. From the filtrate after concentration in vacuo an additional 1.5 g of octahedra was obtained. Total yield of pure octahedra from 7 g of uric acid amounted to 4.5 g.

Found %: C 41.44, 41.26; H 3.34, 3.3; N 23.37, 22.05. $C_{18}H_{18}O_{11}N_6$. Calculated %: C 41.38; H 3.47; N 21.45.

Acetyl groups found, according to Kuhn and Roth [10] in %: 33.47, 33.49. Acetyl groups calculated for an equimolar mixture of (II) and (III), 32.95%.

Investigation of Chemical Properties of Equimolar Mixture of 7-Acetyaluric Acid (II) and 4-Carbacetoxiamino-5-diacetylaminouracil (III).

(a) Reaction with Aniline.

Into a 25 ml flask were introduced 2.7 g (0.005 mole) of the described mixture of (II) and (III), 1.4 g (0.015 mole) of aniline, 10 ml of absolute ether, and with periodic shaking the mixture was left to stand at room temperature for 24 hours. The undissolved precipitate was filtered off, washed with ether, and the ether solution concentrated. After evaporation of ether, the residue was suspended in a small amount of water, the suspension acidified with dilute hydrochloric acid until weakly acid to congo, and filtered. The precipitate washed in this manner was crystallized from water. Yield of pure acetanilide with m.p. 113-115° was 0.5 g. A sample mixed with the authentic substance gave no melting point depression. From the filtrate after crystallization by concentration an additional 0.15 g of acetanilide was obtained. Thus, total yield of acetanilide was 0.65 g (93%).

(b) Hydrolysis with Water.

5.2 g (0.01 mole) of octahedra was boiled for 1 hour in 50 ml of water, 218 ml (97.5%) of carbon dioxide being evolved under normal conditions. The precipitate obtained after hydrolysis was filtered off and boiled in 175 ml of water. Yield of precipitate washed in this manner and dried was 1.4 g. The product obtained was identified as uric acid, with content of pure substance 97.7%. Yield of uric acid 83.5%.

(c) Acidolysis by Acetic Acid in Presence of Dimethylaniline.

In a 100 ml flask fitted with reflux condenser connected to a 500 ml gasometer were placed 5.2 g of octahedra, 50 ml of glacial acetic acid, and 10 ml of dimethylaniline. The mixture was boiled until carbon dioxide evolution ceased, this usually occurring 3 hours after commencement of boiling. During this time, 218 ml (98.0%) of carbon dioxide was evolved under normal conditions. The reaction mixture was cooled, the precipitate filtered off and suspended in 15 ml of water. The resulting suspension was acidified with hydrochloric acid (1:1) until weakly acidic to congo, filtered, and the precipitate washed with water on the filter. Weight of product obtained, which by its composition was a mixture of uric acid and acetyl derivatives of 4,5-diaminouracil, was equal to 2.6 g. On crystallizing from 150 ml of water, 1 g of uric acid was isolated from the mixture obtained as an insoluble precipitate. On cooling the aqueous solution 1.1 g of a mixture separated out, consisting of 4-amino-5-acetylaminouracil (21.15%) and 4,5-diacetylaminouracil (78.85%).*

(d) Acetylation with Acetic Anhydride in Presence of Pyridine Bases and Acetic Acid.

* The percentage content of mono- and diacetyl derivatives of 4,5-diaminouracil in these experiments was determined by conductometric titration by V. F. Degtyarevii.

In a 100 ml round-bottomed flask fitted with reflux condenser connected to a gasometer were placed 5.2 g of octahedra, 16 ml of acetic anhydride, 19 ml of acetic acid, and 10 ml of pyridine bases (b.p. 125-135°). The mixture was heated on an oil bath (oil temperature 135-145°) for 3 hours. After heating was discontinued, the contents of the flask were quickly cooled to room temperature. Volume of gas, brought to normal conditions, was equal to 384 ml (86%).

To hydrolyze excess acetic anhydride in the reaction mixture boiled on an oil bath for 30 minutes. Heating was then discontinued and 50 ml of dichloroethane added. The precipitate settling out was filtered off, washed on the filter with dichloroethane and dried. Weight of precipitate, 3.2 g. On crystallizing from 27 times its amount of water, 0.9 g of insoluble precipitate was obtained, identified as 8-methylxanthine. From the filtrate on cooling, 2 g of 4,5-diacetylamino-uracil settled out. Yield of product, calculated on 8-methylxanthine formed, amounted to about 61%.

SUMMARY

1. The primary reaction products were studied of the reaction of uric acid with acetic anhydride. It was established that acetylation of uric acid proceeds initially with formation of 7-acetyaluric acid.

2. A scheme was proposed for the mechanism of the conversion of uric acid into 8-methylxanthine on reacting it with acetic anhydride.

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SYNTHESIS IN THE PHENOTHIAZINE SERIES

VI. AMINES OF THE PHENOTHIAZINE SERIES

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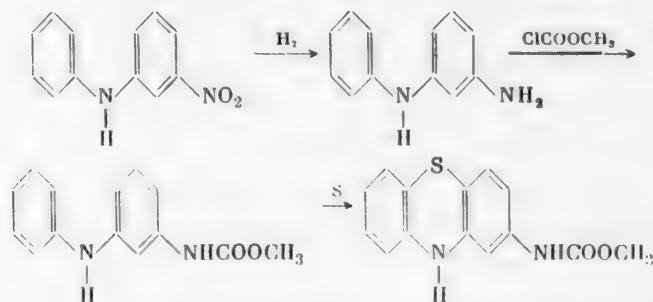
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Continuing our investigation on the synthesis of aminosubstituted phenothiazine [1,2], it was of interest to obtain 2-aminophenothiazine, which is not described in the literature, and use it for subsequent syntheses of substituted phenothiazine to ascertain which compounds are pharmacologically active. We considered this direction of the synthesis desirable, because a number of highly active medicinal preparations were found among the 10-aminoalkyl derivatives of phenothiazine substituted in the 2 position by various groups (see review [3]).

We made attempts to obtain 2-aminophenothiazine by the action of sulfur on 3-aminodiphenylamine under the conditions of sulfurization of other substituted diphenylamines. However, as might be expected, because of the high reactivity of the amino group the reaction products were very tarry and could not be isolated. In subsequent experiments, by the action of the methyl ester of the chlorocarbonic acid 3-aminodiphenylamine was converted to the urethan derivative, from which the methyl ester of phenothiazinecarbamic acid was obtained by sulfurization. Our attempts to saponify the latter have not been successful. This compound was synthesized as follows:



3-Aminodiphenylamine was synthesized by hydrogenation of 3-nitrodiphenylamine (obtained by a method modified by the authors [4], using Raney nickel as catalyst; the product was converted to the methyl ester of diphenyl-3-carbamic acid by the action of chlorocarbonic ester. This ester was converted to the methyl ester of phenothiazine-2-carbamic acid by sulfurization in the presence of catalytic amounts of iodine.

We encountered serious difficulties in our efforts to obtain the urethan derivative of phenothiazine. Direct fusion of the methyl ester of diphenylamine-3-carbamic acid with sulfur in the presence of iodine at 150° or above, in accordance with the standard method of obtaining substituted phenothiazines, was accompanied by intense tarring and we did not succeed in obtaining the expected substance from the tarry reaction products. A small amount of this compound was obtained from the reaction mass by carrying out the sulfurization reaction in xylene, in accordance with the Massie and Kadaba method [5]. As was shown by our experiments, the reaction, carried out by boiling the methyl ester of diphenylamine-3-carbamic acid with sublimated sulfur in the presence of iodine in a small amount of toluene, takes place smoothly, without appreciable tarring, and the unpurified urethan substituted phenothiazine is obtained with a yield of 73.5%. One recrystallization from aqueous acetone, and then from alcohol or toluene, gives a substance with a constant melting point.

We assumed that the structure of the methyl ester of phenothiazine-2-carbamic acid is the most probable because when all the other hitherto-known diphenylamines substituted in the 3 position react with sulfur, 2-substituted

phenothiazines are obtained as the main reaction product, whereas only a negligible amount of the isomeric derivative of phenothiazine (substituted in the 4 position) is formed [6-9]. This is evidently the reason for the fact that we did not succeed in establishing the presence of the second isomer, i.e. the methyl ester of phenothiazine-4-carbamic acid. By means of acid or alkaline saponification of the methyl ester of phenothiazine-2-carbamic acid we made attempts to obtain 2-aminophenothiazine and prepare the already-known 2-chlorophenothiazine by replacing the amino group by chlorine. However, under mild saponification conditions this urethan substituted phenothiazine was stable to hydrolysis. Under severer saponification conditions, black insoluble substances which cannot be isolated are obtained; this is evidently due to the instability of 2-aminophenothiazine under the given conditions. Investigations in this direction are being continued.

EXPERIMENTAL

3-Nitrodiphenylamine. 325 g of 3-nitroacetanilide, 300 g of bromobenzene, 133 g of anhydrous potash, 10 g of freshly prepared copper powder (obtained from a solution of copper and zinc sulfates [10]), 1 g of potassium iodide and 100 g of nitrobenzene were placed in a 3-liter three-necked flask equipped with a stirrer, thermometer and reflux air condenser (length 70-75 cm) and boiled while stirring for 20 hours. In the first 10 hours the temperature of the reaction mixture was increased from 160 to 180°, and was then increased to 210° in the next 10 hours. During the reaction a further 270 g of bromobenzene was added in amounts which allowed the temperature of the reaction mixture to be kept within the indicated limits. The water formed during the reaction distilled gradually through the air condenser. After the reaction had ended, the nitrobenzene and the excess bromobenzene were steam distilled. The water was decanted from the tar, it was dissolved in 1.5 liters of alcohol, 70 ml of concentrated hydrochloric acid (d 1.19) was added and the mixture was boiled for 5 hours. The dark-red precipitate which separated out on cooling was filtered and dried. We obtained 265 g (69.5% with respect to 3-nitroacetanilide) of 3-nitrodiphenylamide with a m.p. of 106-108°; when this was recrystallized twice from aqueous alcohol, a ruby-red crystalline substance with a m.p. of 113-114° was obtained. In the literature [4-11] the m.p. is given as 114°.

3-Aminodiphenylamine. A suspension of 50 g of 3-nitrodiphenylamine in 350 ml of alcohol was reduced by hydrogen in the presence of 30 g of Raney nickel. The reduction took place with considerable evolution of heat by the mixture. With an increase in reduction, the 3-nitrodiphenylamine dissolved, forming a dark transparent solution. In 2-3 hours, almost the theoretical amount of hydrogen was absorbed. The catalyst was filtered, the alcohol was distilled from the filtrate. The sirupy residue was dissolved in 10-15% hydrochloric acid and cooled. The precipitate which separated was filtered, washed with cold water and dried. We obtained 48 g (83%) of 3-aminodiphenylamine hydrochloride (m.p. 223-225°). After recrystallization from alcohol it melted at 235-236°; the colorless lustrous needles were readily soluble in hot water and in alcohol. The 3-aminodiphenylamine base, obtained from the hydrochloride by treatment with alkali and recrystallizing from aqueous alcohol, melted at 72-74° (m.p. 76-77° [12]).

Methyl ester of diphenylamine-3-carbamic acid. 22.45 g of 3-aminodiphenylamine hydrochloride was dissolved in 100 ml of alcohol and a solution of 4 g of caustic soda in 20 ml of alcohol was added. 9.5 g and then a further 9.4 g of the methyl ester of chlorocarbonic acid was added dropwise with stirring to the cooled (10-15°) solution. A solution of 10.6 g of sodium carbonate in 50 ml of water was added dropwise at the same time as the second portion of ester. After the ester and the sodium carbonate solution had been added to the reaction mixture, 50 ml of water was added and the mixture was heated for 1 hour, the temperature being kept between 10 and 15°. The precipitate which separated was washed with a small amount of cold water and dried. We obtained 22.8 g (95% with respect to 3-aminodiphenylamine hydrochloride) of unpurified substance with an m.p. of 102-103°. After this had been recrystallized twice from alcohol it melted at 112-113°; the colorless lustrous plates were readily soluble in alcohol and soluble with difficulty in hot water.

Found %: N 11.79, 11.74. $C_{14}H_{14}O_2N_2$. Calculated %: N 11.56.

Methyl ester of phenothiazine-2-carbamic acid. 2.42 g of the ethyl ester of diphenylamine-3-carbamic acid, 0.96 g of sublimated sulfur and a small iodine crystal were boiled in 4-5 ml of toluene until liberation of hydrogen sulfide had ceased. The reaction mass was dissolved by adding a small amount of toluene and boiling; the excess sulfur was filtered and a fine, yellow crystalline precipitate separated out when the filtrate was cooled. After the precipitate had been filtered and dried, it melted at 178-180°; the weight was 2 g (73.5%, calculated on the initial ester). Recrystallization from aqueous acetone (with addition of activated carbon) and then from alcohol gave fine lustrous plates with a very faint greenish tint; the m.p. was 217-218°. The substance was very readily soluble in acetone, hot toluene and alcohol; it was almost insoluble in water.

Found %: C 62.31, 62.23; H 4.41, 4.46; N 10.46, 10.47. $C_{14}H_{12}O_2N_2S$. Calculated %: C 61.74; H 4.45; N 10.29.

SUMMARY

A new substituted phenothiazine, the methyl ester of phenothiazine-2-carbamic acid, was synthesized by sulfuration of the methyl ester of diphenylamine-3-carbamic acid in toluene.

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RADICAL REACTIONS OF PERCARBONATES

II. DECOMPOSITION OF DICYCLOHEXYL PEROXYDICARBONATE

IN BENZENE AND ACETIC ACID IN THE PRESENCE OF METALS

AND METAL SALTS*

L. M. Terman and G. A. Razuvaev

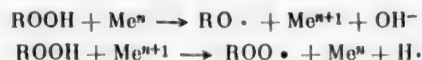
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Original article submitted September 30, 1961

The effect of various metals on the decomposition of symmetrical and unsymmetrical acyl peroxides has been fairly closely investigated [1-3]. In the presence of metals the rate of decomposition of the peroxide increases considerably and the temperature barrier of the reaction is reduced. Thus, in the case of the decomposition of benzoyl, acetylbenzoyl and phenacylbenzoyl peroxides in a number of solvents in the presence of Na, Zn, Fe, Ni, Cu, Hg, Ag and Pt the reaction is fully completed in 2-3 hours at room temperature [2], whereas in the absence of a metal, decomposition took several hours at the boiling point of the solvent.

Analysis of the reaction products showed that in many cases the radicals formed during the decomposition of peroxides react with the metals, giving the corresponding salts. Metal salts were also formed during the decomposition of benzene diazo-acetate [3] in the presence of Zn, Fe, Cu and Hg.

Salts of metals of variable valence modify substantially the decomposition mechanism of hydroperoxides [4]; these authors assume that the hydroperoxide acts as an oxidizer and a reducer alternately.



Kharasch explains the effect of cobalt salts on the decomposition of tertiary-butyl hydroperoxide in a similar way [5]. Small amounts of copper salts cause a substantial change in the mechanism of the reaction of certain peroxides with the solvent. In the presence of 1 mole of copper chloride, benzoyl and tertiary-butyl peroxide, tertiary-butyl perbenzoate, tertiary-butyl hydroperoxide and 2-cumyl hydroperoxide undergo rapid induced decomposition in solvents in which, in the absence of copper chloride, they undergo slow decomposition in a 1st order reaction, or are not decomposed at all [6].

The reactions which certain metal salts undergo when acted on by peroxides are of interest [7]. In the presence of small amounts of acetyl or benzoyl peroxide the decarboxylation reaction of mercury salts takes place with the formation of the corresponding organometallic compounds.

We considered it of interest to investigate the effect of metals and metal salts on the decomposition of peroxydicarbonates in solutions.

Preliminary experiments established that at room temperature dicyclohexyl percarbonate is not decomposed in benzene (0.33 mole/liter) in the presence of a number of metals. For this reason, we checked the effect of metals on the rate of decomposition of dicyclohexyl percarbonate in benzene with heating. Data on the decomposition of the percarbonate in benzene at 50° in the presence of Pt, Cu, Ag, Al, Zn, Ni and Hg are given in Table 1.

From the data of Table 1 it is evident that in the presence of Pt and Cu the rate of decomposition of peroxide increases considerably. The effect of other metals is somewhat weaker.

* For communication I, see [8].

TABLE 1. Decomposition of Dicyclohexyl Percarbonate in Benzene in the Presence of Metals (c_0 0.03 g-mole/liter, 50°, 3 hours)

	Without additions	Pt	Cu	Hg	Al	Fe	Ni	Ag
Peroxide decomposed (%)	55.25, 53	100	100	85.1	76.5	77	66.6	66.2

The products formed as a result of the decomposition of peroxide in benzene in the presence of these metals were investigated. It was previously established [8] that during the decomposition of percarbonates in benzene the radicals formed as a result of the decomposition of the peroxide do not detach hydrogen from the solvent, but are subjected to disproportionation reactions. Diphenyl, which may be formed by dimerization of the phenyl radicals obtained as a result of removal of hydrogen from the benzene molecules, was not found. It was assumed that in the presence of metals the mechanism of the reaction of the peroxide with the solvent may vary; furthermore, it could be expected that products of the reaction of RO^\cdot -radicals with the metals would appear. Data on the decomposition of dicyclohexyl percarbonate in the presence of Pt, Hg, Cu, Zn and Al are given in Table 2.

TABLE 2. Products of the Thermal Decomposition of Dicyclohexyl Percarbonate in Benzene in the Presence of Metals at 60-70° (c_0 0.3 g-mole/liter)

Metal	Decomp. time, hrs.	$C_6H_{11}OH$	$C_6H_{10}O$	CO_2 In mole/ liter	Total balance, taking into account A, [8]
		In moles per mole of decomposed pero.			
nonmetal	50	0.98	0.245	1.8	91.4
Pt	4	0.99	0.35	1.84	94.9
Cu	4	0.78	0.34	1.78	94.9
Hg	7	0.79	0.42	1.74	—
Al	8	1.04	0.36	1.81	95.7
Fe	12	0.78	0.34	1.74	—
Zn	24	1.08	0.37	1.71	—

From the data of Table 2 it is evident that both with and without metals the main reaction products are cyclohexanol, cyclohexanone and carbon dioxide. When the reaction had ended, an analysis was carried out for the ions of the corresponding metals but they were not detected. In addition, the amount of metal used in the reaction was checked in every experiment. The metal was regenerated completely, and in the same form in which it was used for the reaction. The solutions did not become colored as a result of the decomposition of percarbonate in the presence of metals. Diphenyl was not found in the reaction products. Therefore, no changes took place in the composition of the products during the decomposition of dicyclohexyl percarbonate in benzene with additions of metals. The reaction mechanism of the decomposition of percarbonates is evidently unchanged in the presence of these metals. The increase in the decomposition rate may be explained by the fact that in this case the reactions take place on the surface of the metals.

The presence of free radicals during the decomposition of percarbonates in solution is confirmed by the decarboxylation reaction of mercuric acetate. The reaction was carried out in benzene and in glacial acetic acid, preliminary experiments having established that during decomposition in the latter, peroxide radicals are subjected only to disproportionation reactions. Succinic acid, which could be formed by dimerization of the radicals formed as a result of removal of hydrogen from acetic acid molecules, was not obtained. Therefore the system contains no other radicals except those which occur as a result of the decomposition of the percarbonate. It could therefore be assumed that if such radicals are formed, a chain reaction of the decarboxylation of mercuric acetate must take place.

The decarboxylation reaction was carried out in solutions of benzene and glacial acetic acid. Methylmercuric acetate (in the form of methyl mercuric iodide), small amounts of mercurous acetate and carbon dioxide were obtained. The results of the experiments are given in Table 3.

TABLE 3. Decomposition of Mercuric Acetate, Induced by Dicyclohexyl Percarbonate in Glacial Acetic Acid

Peroxide sample (g-mole)	Sample of mercuric acetate (g-mole)	Relation temperature	Yield of mercuric acetate		Yield of mercurous acetate of mercurous oxide	
			in g-mole	as a % of the initial amount of mercury salt	in g-mole	as a % of the initial amount of mercury salt
0.01	0.09	98°	0.076	83.2	0.012	12.5
0.01	0.09	80	0.057	63	0.016	17.5

As may be seen from the data of Table 3, the yield of methyl mercuric acetate is high, being far more than 100%, calculated on the peroxide. This indicates that a chain radical process, initiated by percarbonate, takes place.

The decarboxylation reaction of the mercuric acetate was carried out in benzene; however, the yield of the main product, methyl mercuric acetate, was low, as in the case of experiments with acetyl and benzoyl peroxides [7].

EXPERIMENTAL*

Initial substances. Dicyclohexyl peroxydicarbonate was synthesized from cyclohexyl chloroformate [9], purified by reprecipitation from acetone into water and was used in the reaction as a 100% pure product. The peroxide was analyzed iodometrically [10]. The benzene was purified by a known method [11]. Pt, Ag, Cu, Ni, Al, Zn and Fe were used in the freshly precipitated, pure [12] form, as a paste in benzene or a dry powder; the mercuric acetate was synthesized according to [12].

Rate of decomposition of dicyclohexylperoxydicarbonate in benzene in the presence of metals. The reaction was carried out in sealed ampoules containing 10 ml of a benzene solution of the percarbonate (0.03 g-mole/liter) and 1 g of the corresponding metal. The ampoules were shaken for 3 hours at 50°. They were then frozen in a mixture of dry ice and acetone and opened; the metal was filtered and the amount of undecomposed peroxide in the filtrate was determined iodometrically.

Reaction of the thermal decomposition of dicyclohexylperoxydicarbonate in benzene in the presence of metals. The decomposition of the dicyclohexyl percarbonate in benzene (0.3 g-mole/liter) in the presence of metals (1-2 g per 100 ml of solution) was carried out in an atmosphere of purified nitrogen at 60-70°, with constant and vigorous stirring. The reaction was carried out in a round-bottomed flask, equipped with a reflux condenser, connected by means of a ground-glass joint; a potash bulb system with a 30% solution of alkali was attached to the upper end of the condenser. The end of the reaction was determined by carrying out a test for peroxide.

When the reaction had ended, the metal precipitate was filtered, washed with benzene and weighed. The ions of the corresponding metals in the filtrate were determined [13]. The benzene was distilled from the filtrate, the residue was weighed and was analyzed for cyclohexanol content [14] and cyclohexanone [15]. The latter was identified as the 2,4-dinitrophenylhydrazone (m.p. 162°; a mixed melt showed no depression of the melting point). After samples had been taken, the residue was steam distilled. Diphenyl was not found. The amount of CO₂ was determined by the increase in weight of the potash bulbs.

Decomposition reaction of dicyclohexyl peroxydicarbonate in glacial acetic acid. 3 g of dicyclohexyl percarbonate in 20 ml of CH₃COOH was added in small amounts to 25 ml of CH₃COOH, heated to 90°. After all the peroxide had been added, heating was continued for another 2 hours. During this period the peroxide decomposed completely. The main part of the acetic acid was distilled from the reaction mixture at 44-45° (45 mm). After the acetic acid had been driven off, the residue was left overnight. Crystallization was not observed. The mixture was treated with a concentrated soda solution. Succinic acid was not precipitated when the soda solution was acidified. Since decomposition took place very vigorously, in some experiments the temperature was reduced to 55°. However, in this case we did not succeed in precipitating succinic acid.

* I. K. Potatueva took part in the work.

Reaction of dicyclohexylperoxydicarbonate with mercuric acetate in glacial acetic acid. 29.4 g (0.086 mole) of the mercuric acetate, 3 g (0.01 mole) of percarbonate, 115 ml of glacial acetic acid and 2 ml of acetic anhydride were placed in the reaction flask. The reaction was carried out at 80 and 98°. The end of the reaction was determined by testing for peroxide. The reaction last 1 hour; when it had ended, the solution was separated on a Buchner funnel from the white flaky precipitate formed during the reaction. The precipitate was difficultly soluble in water, insoluble in alcohol, and gave quantitative reactions for the Hg_2^{++} ion [13]. When an attempt was made to determine the melting point, the crystals decomposed at 183-185°. The precipitate was identified as mercuric acetate.

After the mercuric acetate had been separated, the filtrate was diluted with water and a fine-crystalline precipitate, which was identified as methyl mercuric iodide, was precipitated from it by a KI solution. The m.p. was 145°; a mixed melt with pure methyl mercuric iodide showed no depression of the melting point.

SUMMARY

1. Additions of metals accelerate the decomposition of dicyclohexylperoxydicarbonate in solution. Such additions do not change the reaction mechanism of decomposition.
2. Dicyclohexylperoxydicarbonate induces a chain reaction of decarboxylation of mercuric acetate.

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THE ABSORPTION SPECTRA OF CERTAIN THIOPYRIDONES IN PYRIDYL SULFIDES

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The investigation of the absorption spectra of mercapto-pyridone derivatives and their oxygen analogs is of interest from both the theoretical and the practical aspect. The chemical and physicochemical properties of compounds of this group are mainly explained satisfactorily within the limits of present theories; however, there are still a number of unsolved problems concerning the molecular structures of these substances. As regards spectroscopic investigations, data are either incomplete or of an unsystematic character.

The absorption spectra of hydroxypyridones and their derivatives have been investigated repeatedly, both in the infrared and ultraviolet regions of the spectrum [1-5]. These investigations showed that in neutral media, 2- and 4-pyridones have the structure of pyridones. According to x-ray structural data [6], crystalline 2-pyridone has the same structure. However, chemical investigations showed that the C = O group of pyridones does not have a clearly expressed ketonic character and is more similar to carbonyls of amides. For this reason it is assumed that the structure of pyridones is intermediate between the pyridone and bipolar type.

The chemical properties of thiopyridones are a more positive indication of the thioketonic character of the C = S group [7]. An x-ray investigation of 2-thiopyridone [8] also indicates that it has a thionic, not a thiolic structure. There is some confirmation of this in spectroscopic investigations [9-11], but unfortunately the number of such investigations is still limited.






Two reports on the investigation of ultraviolet absorption spectra of thiopyridones and their derivatives have been published. Ross [10] showed that the absorption spectra of solutions of 4-thiopyridone in the 220-400 m μ region agree with the thionic structure of its molecule. In an alcoholic solution of 4-thiopyridone he observed bands with maxima near 220-225, 297 and 341 m μ . In [11] Jones Katritzky investigated the absorption spectra of 2- and 4-thiopyridones and their methyl and benzyl substituents in the near ultraviolet region, in connection with the problem of the basicity of these compounds. The authors limited their investigation to absorption spectra in acid and basic media only, with use of phosphate buffers. The complex character of the investigated mixtures and the differences in the solution concentrations and pH values impede the interpretation of the measurement results and, in the authors' opinion, are the cause of the erroneous allocation of the absorption bands. Nevertheless, as indicated by Jones and Katritzky, their data also confirm the thionic structure of 2- and 4-thiopyridones.

In the present work the ultraviolet absorption spectra of solutions of 2- and 4-mercaptopyridines and a number of their derivatives (the synthesis of the substances will be described in another report) were investigated. The absorption spectra were obtained by means of an SF-4 spectrophotometer. The error of the determination of λ_{\max} is 5 Å. The mean error of measurements of λ_{\max} is 1.5%. All the substances were carefully purified by distillation or crystallization. The spectra were measured in alcoholic solutions.

In general, the data obtained agree satisfactorily with the results of measurements obtained by Ross and by Jones and Katritzky, although a direct comparison with the latter work is difficult in view of the differences in the measurement conditions.

As may be seen from the data of table and figure, the absorption spectra in the 200-400 m μ region of each of the investigated compounds consists of two-three intense bands. It is readily noted that all the observed spectra are clearly divided into four types (the names are conventional).

Maxima of Absorption Bands of Alcoholic Solutions of Mercaptopyridine Derivatives in the 200-400 m μ Region

No. of curve in fig.	Type of compound	R	Name of compound	Solution conc. (m)	λ_{\max} (in m μ) (ϵ_{\max} in liter \cdot mole $^{-1}$ cm $^{-1}$, 10^4)
1	2-Mercaptopyridine type 	CH ₃ CH ₂ COOH	β -Carboxyethyl (2-pyridyl) sulfide	0.014	248.8 (9.5) 291.0 (4.3)
2		CH ₃	Methyl (2-pyridyl) sulfide	0.030	249.0 292.5
3		CH ₃ CH ₂ CN	β -Cyanoethyl (2-pyridyl) sulfide	0.030	245.0 287.5
4	4-Mercaptopyridone type 	CH ₃ CH ₂ CN	β -Cyanoethyl (4-pyridyl) sulfide	0.015	215.5 (9.4) 260.0 (12.9) 341.5
5		CH ₃ CH(CH ₃)COOCH ₃	β -Carbomethoxypropyl (4-pyridyl) sulfide	0.015	216 263 341
6	2-Thiopyridine type 	CH ₃ CH ₂ CN	N-(β -cyanoethyl)-2-thiopyridone	0.030	200 * 286.0 (10.3) 361.5 (5.8)
7		CH ₃ CH ₂ COOH	N-(β -Carboxyethyl)-2-thiopyridone	0.027	200 * 287.5 (8.2) 358.5 (4.7)
8		H	2-Thiopyridone	0.010	200 * 284.0 (12.1) 360.0 (5.75)
9	4-Thiopyridone type 	CH ₃	N-Methyl-2-thiopyridone	0.010	210 (8.7) 284.0 (11.0) 355.0 (6.0)
10		CH ₃ CH(CH ₃)COOCH ₃	N(β -Carbomethoxypropyl)-4-thiopyridone	0.010	233.0 (6.3) 348.2 (23.3)
11		H	4-Thiopyridone	0.010	231.0 (6.9) 338.2 (17.4)
12		CH ₃ CH ₂ CN	N-(β -Cyanoethyl)-4-thiopyridone	0.030	233.0 (6.6) 349.0 (26.2)

* The longwave portion of the absorption band was measured.

1. The 2-mercaptopyridine type. This is characterized by two intense bands: 245-250 m μ ($\epsilon \sim 10^4$) and 287-293 m μ ($\epsilon \sim 4 \cdot 10^3$). The third band has a maximum below 200 m μ (the longwave portion was measured in part).

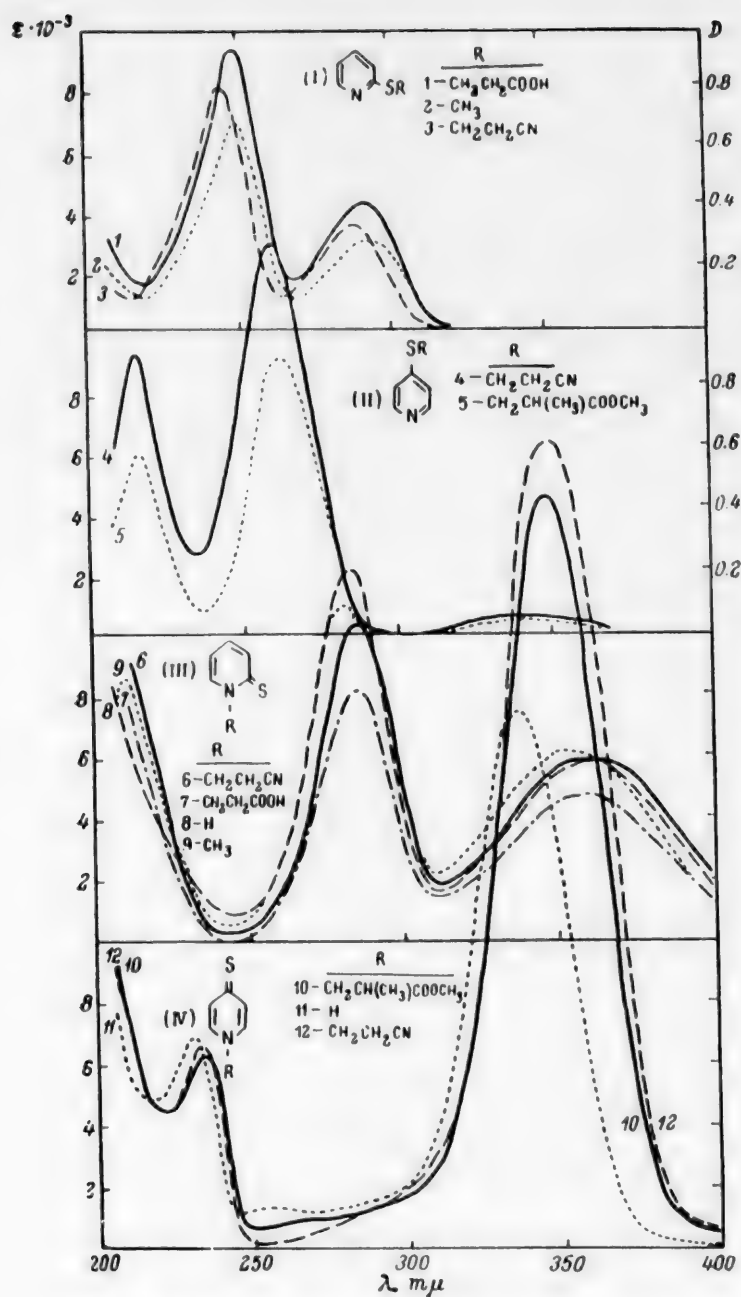
2. The 4-mercaptopyridine type. Characterized by three bands: 215-216 m μ ($\epsilon \sim 10^4$), 260-263 m μ ($\epsilon \sim 1.3 \cdot 10^4$) and 340-342 m μ ($\epsilon \sim 500$).

3. The 2-thiopyridone type. Characterized by three bands: one at about 200 m μ (ϵ is evidently of the order of 10^4 ; the longwave portion was measured); two others at 283-286 m μ ($\epsilon \sim 10^4$) and 355-363 m μ ($\epsilon \sim 5 \cdot 10^3$).

4. The 4-thiopyridone type. Characterized by the following bands: 231-238 m μ ($\epsilon \sim 6 \cdot 7 \cdot 10^3$) and 338-350 m μ ($\epsilon \sim 2 \cdot 10^4$); the third band has a maximum at about 200 m μ (the longwave portion was measured).

The very satisfactory agreement of the spectra of compounds belonging to the same type is noteworthy. This indicates that the spectral picture is determined mainly by the point of substitution, but that the character of the substituent does not have an important effect on the position and intensity of the absorption band.* Although this conclusion is not unexpected, it has not been corroborated previously for this class of compound.

* A similar conclusion for alkyl pyridines was drawn in [12] by Podall.



Absorption spectra of mercaptopyridines in thiopyridines in ethyl alcohol. For curves 2, 3 and 5 the value $D = \log(I_0/I)$ is plotted on the ordinate.

Both the position and the intensity of the main absorption bands of compounds of the 1st and 2nd types indicate that the pyridine ring of these compounds basically retains its aromatic character, but that differences in the electronic structure of the ring (deformations of the electron shell) are shown in displacements of the bands and a certain change in their intensities. The absorption bands of substances of the 3rd type (2-thiopyridone type) are dis-

placed considerably with respect to bands of the 1st type, which is undoubtedly due to serious changes in the electron structure of the pyridine ring. However, another fact, which, in our opinion, is no less important, should be noted: the undoubted similarity in the general character of the absorption curves (intensity, the half-width of the bands, the form of the outlines) of compounds of the 1st and 3rd types. In the present case this similarity is evidently explained by the fact that the basic structural characteristics of the pyridine ring are retained for compounds of the 2-thio-pyridone type, although a certain displacement towards the thionic structure takes place as a result of the influence of the $C=S$ group. In turn, the $C=S$ group does not have a thioketonic character, but evidently has a structure intermediate between the limiting cases of thioketonic and bipolar structures.

The absorption spectra of the 4th group of compounds (4-thiopyridone type) are completely different from those described above. Here, the very intense band in the 340-350 $m\mu$ region ($\epsilon \sim 18-26 \cdot 10^3$) is primarily noteworthy. The presence of this band may be interpreted in one way only: the pyridine ring of compounds of the 4-thiopyridone type (in alcoholic solutions) loses its aromatic character. The intense longwave band indicates that molecules of these compounds have a thioquinoid structure. Naturally, the presence of a heteroatom in the ring is bound to leave its mark on the molecular structure; here, too, a certain displacement towards the bipolar structure may probably occur. Nevertheless, there is no doubt that the thioketonic character of the $C=S$ group must be expressed far more markedly for 4-thiopyridone derivatives than for 2-thiopyridone derivatives. All this is obviously also true for 2- and 4-thiopyridone themselves.

It is interesting to note that in solutions of certain compounds of the 4th group (for example, N-(β -carbo-methoxypropyl)-4-thiopyridone), a 290 $m\mu$ band and a prominence at 240 $m\mu$ appear with an increase in concentration. This is probably due to the presence of ionic forms in the solution. The 297 $m\mu$ band observed by Ross in an alcohol solution of 4-thiopyridone has the same origin.

SUMMARY

1. The absorption spectra of alcoholic solutions of twelve compounds - 2- and 4-thiopyridone and their derivatives - in the 200-400 $m\mu$ region were measured (eight of them for the first time).
2. It was shown that in the absence of conjugation between the substituent and the pyridine ring, the character of the spectrum is determined mainly by the point of substitution and is independent of the type of substituent.
3. It was established that there is a marked difference between the spectra of 4-thiopyridone and its derivatives and the spectra of the other compounds; this indicates that there are serious differences in the electron structure of both the pyridine ring and the $C=S$ groups in these compounds and compounds of the 2-thiopyridone type (displacement towards a thioquinone structure).

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LETTERS TO THE EDITOR

A NEW TYPE OF CONDENSATION OF 2-HYDROXY- 2,5-DIHYDROFURANS

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Translated from *Zhurnal Obshchei Khimii*, Vol. 31, No. 9,

pp. 3141-3142, September, 1961

Original article submitted May 28, 1961

Continuing our investigation of conversions of pinacones with substituted acetylene radicals [1], we studied the action of 25% sulfuric acid on unsymm. dimethyl-phenyl-allylenylethylene glycol (2-methyl-3-phenyl-hexine-4-2,3-diol) (I) with heating. During this investigation, two substances were isolated.

1) A diene ketone - 2-methyl-3-phenylhexa-1,3-diene-5-one (II) - a mobile light-yellow liquid of pleasant odor, with a b.p. of 78-80° (2.5 mm), n_D^{20} 1.5130.

Found %: C 83.58; H 8.02. M 172. $C_{13}H_{14}O$. Calculated %: C 83.87; H 7.52. M 186.

Infrared spectrum: 1685 (conjugated carbonyl group); 1596 (conjugated diene bonds); 954 (isopropenyl group); 913, 971 cm^{-1} (methylene group).

The 2,4-dinitrophenylhydrazone is yellow-orange; the m.p. is 155-157° (from alcohol).

Found %: N 15.70. $C_{19}H_{18}O_4N_4$. Calculated %: N 15.30.

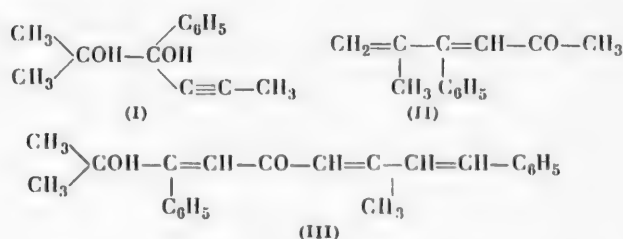
2) A triene γ -keto alcohol - 2,7-dimethyl-3,9-diphenylnona-3,6,8-triene-2-ol-5-one (III) - a very viscous yellow-red liquid with a b.p. of 134-136° (0.8 mm), n_D^{20} 1.5832.

Found %: C 83.17; H 7.60; OH 0.22. M 326. $C_{23}H_{24}O_2$. Calculated %: C 83.10; H 7.60; OH 0.30. M 332.

Infrared spectrum: 1650 (conjugated carbonyl group); 3375 and 3420 cm^{-1} (associated hydroxyl group).

The 2,4-dinitrophenylhydrazone is yellow, the m.p. is 223° (from glacial acetic acid).

Found %: C 67.95; H 5.79; N 10.95. $C_{29}H_{28}O_5N_4$. Calculated %: C 67.97; H 5.51; N 10.94.



The formation of compounds (II) and (III) may be explained by the conversion of the acetylene α -glycol (I) by sulfuric acid to 2,5-dihydrofurylium sulfate, which as a result of partial hydrolysis forms free hydroxydihydrofuran (2,5,5-trimethyl-4-phenyl-2-hydroxy-2,5-dihydrofuran, M 204). This hydroxydihydrofuran is converted to the tautomeric form of the ethylene γ -keto alcohol, which changes in two directions: as a result of dehydration the diene ketone (II) isolated by the authors is obtained, while with ketone splitting, benzalacetone is obtained.

Taking into account the increased mobility of the hydrogen atoms of a methyl group in the α -position in 2,5-dihydrofurylium salts and, therefore, the capacity of these substances to condense with carbonyl compounds, it may be assumed that dihydrofurylium sulfate reacts with benzalacetone and that the corresponding salt of the condensation

product - substituted 2-hydroxy-2,5-dihydrofuran (M 332) - is formed. When the reaction mixture is neutralized, the tautomeric form of this hydroxydihydrofuran, i.e., triene γ -keto alcohol (III), is precipitated.

The ozonolysis products - acetone, dimethylbenzoyl carbinol, acetic, benzoic, pyroracemic and oxalic acid - confirmed the proposed structure of this γ -keto alcohol (III).

Similar condensations for salts of hydroxyphthalanes [2] and for pyrilium salts [3] are described in the literature.

Therefore, in addition to previously investigated condensation of 2-hydroxy-2,5-dihydrofurans by the active hydroxyl group with compounds containing mobile hydrogen atoms [4], we discovered a new type of condensation by way of example of 2,5,5-trimethyl-4-phenyl-2-hydroxy-2,5-dihydrofuran, which takes place in an acid medium as a result of the mobile hydrogen atoms of the methyl group in the position of the 2-heterocyclic group.

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REACTION BETWEEN THE OXIDE OF ERUCIC ACID
METHYL ESTER AND ACETIC ACID

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We have established that when the oxide of erucic acid methyl ester reacts with glacial acetic acid a mixture of the methyl esters of 13-hydroxy-14-acetoxy and 14-hydroxy-13-acetoxybehenic acid, with an m.p. of 53-54°, is formed.

A mixture of the methyl esters of hydroxyacetoxybehenic acids was acted on by phosphorus pentabromide, with subsequent formation of the corresponding methyl esters of bromoacetoxybehenic acids. By elimination of bromine a mixture of the methyl esters of acetoxybehenic acids was obtained; this was chromatographed on neutral aluminum oxide of 3 activity. As a result we obtained 65% of the methyl ester of 13-acetoxybehenic acid with an m.p. of 13-14° and 35% of the methyl ester of 14-acetoxybehenic acid with an m.p. of 15-15.5°. The position of the acetoxy groups was proven by saponification of the methyl esters of acetoxybehenic acids and by comparison of the properties of hydroxybehenic acids with the properties of known 13-hydroxy and 14-hydroxybehenic acids.

Therefore it was established that when the oxide of this ester reacts with glacial acetic acid, the rupture of the oxide ring takes place in two directions, primarily on the side of the (2 : 1) ester group.

DETERMINATION OF THE STRUCTURE OF ABIENOL

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p. 3143, September, 1961

Original article submitted April 6, 1961

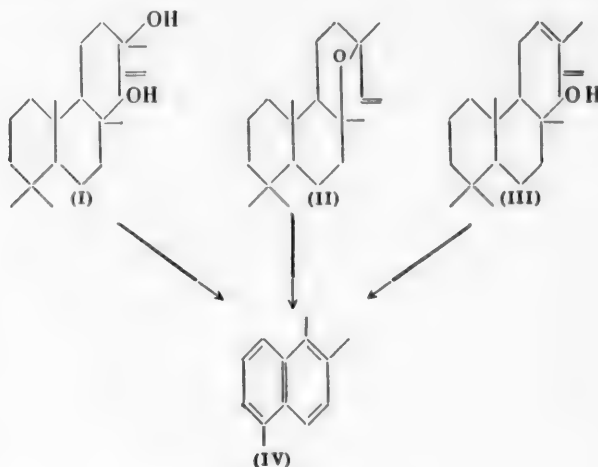
In 1959 we found that in spite of the data of Wienhaus and Mucke [2], the formula $C_{20}H_{34}O$ must be attributed to abienol and, therefore, abienol hydrate must have the formula $C_{20}H_{36}O_2$.

As a result of further investigations we obtained tetrahydroabienol with the formula $C_{20}H_{38}O$: m.p. 48.5-49.5° and $[\alpha]_D - 10.28^\circ$.

By dehydration of the latter we obtained tetrahydroabiene $C_{20}H_{36}$. Dehydrogenation of tetrahydroabiene by means of selenium gives an aromatic hydrocarbon, 1,5,6-trimethylnaphthalene (IV), characterized by the picrate with m.p. 137-139°.

As is known [3,4], this hydrocarbon (IV) was obtained from sclareol (I) and from manool oxide (II) by dehydrogenation by means of selenium. Abienol evidently has a structure similar to that of the above-mentioned compounds.

Our proposed formula for abienol (III) takes into account the presence of a conjugated system of double bonds, a vinyl group and a tertiary hydroxyl.



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ADDITION OF COMPOUNDS OF TRIVALENT PHOSPHORUS CONTAINING A P - Cl BOND TO DIENE HYDROCARBONS

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Original article submitted April 28, 1961

In a number of investigations by our laboratory it was shown that 1,3-diene hydrocarbons add halogen derivatives in the presence of Gustavson catalysts [1]. We established that these catalysts assist the addition of compounds of trivalent phosphorus, containing a P-Cl bond, to 1,3-dienes.

Thus, for example, when divinyl, isoprene, piperylene and chloroprene were heated with the acyl chloride of propylene glycol phosphorous acid to 100-120° in the presence of zinc chloride, the corresponding addition products were obtained with a yield of up to 65%. In contrast to reactions with halogen derivatives, telomerization was not observed in this case.

Addition product of $C_3H_6O_2PCl$ and divinyl (I).

B.p. 147-148° (10 mm), d_4^{20} 1.2369, n_D^{20} 1.4978, MR 46.03; calc. 46.47.

Found %: C 43.23, 43.27; H 6.33, 6.38; P 15.75, 15.80; Cl 18.34, 18.27. $C_7H_{12}O_2PCl$. Calculated %: C 43.16; H 6.16; P 15.92; Cl 18.24.

Addition product of $C_3H_6O_2PCl$ and isoprene (II).

B.p. 155-156° (10 mm), d_4^{20} 1.1881, n_D^{20} 1.4948, MR 51.17; calc. 51.09.

Found %: C 46.37, 46.48; H 6.80, 6.74; P 14.87, 14.67; Cl 16.91, 16.98. $C_8H_{14}O_2PCl$. Calculated %: C 46.06; H 6.70; P 14.87; Cl 17.00.

Addition product of $C_3H_6O_2PCl$ and piperylene (III).

B.p. 144-146° (10 mm), d_4^{20} 1.1850, n_D^{20} 1.4908, MR 50.94; calc. 51.09.

Found %: C 45.85, 45.87; H 6.86, 6.79; P 15.10, 15.05; Cl 17.04, 17.10. $C_8H_{14}O_2PCl$. Calculated %: C 46.06; H 6.70; P 14.87; Cl 17.00.

Addition product of $C_3H_6O_2PCl$ and chloroprene (IV).

B.p. 169-170° (10 mm), d_4^{20} 1.3327, n_D^{20} 1.5130, MR 51.62; calc. 51.37.

Found %: C 36.98, 36.76; H 5.00, 4.94; P 13.47, 13.31; Cl 31.17, 31.14. $C_7H_{11}O_2PCl_2$. Calculated %: C 36.67; H 4.80; P 13.53; Cl 30.96.

All the addition products are resistant to atmospheric oxygen, do not add sulfur, do not react with Cu_2Cl_2 , and add only one mole of bromine (at the double bond), i.e., they are derivatives of pentavalent phosphorus - esters of dialkyl phosphinic acids. The atomic refraction of phosphorus in these compounds is about 4.8, and not 8.5 as in esters of dialkyl phosphinous acids. Arbuzov regrouping [2] evidently takes place during the addition process. Since the addition products give a negative result for primary chlorine by the Somme-Lééts method [3], they, like addition products of PCl_5 [4], are evidently formed by 1,2-addition.

In the infrared spectra, the 1622 (I), 1644 (II), 1610 (III) and 1624 (IV) cm^{-1} bands correspond to the double bond, and bands up to 3051 cm^{-1} to CH valence vibrations, which also indicates the presence of end double bonds. Very intense bands of about 1250 cm^{-1} correspond to the P = O group. The 900-1000 cm^{-1} region could not be used for determining the structure because of the superposition of the ring frequencies.

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THE ACYLATION OF ORGANIC COMPOUNDS BY ACYL
CHLORIDES OF CARBOXYLIC ACIDS IN THE PRESENCE
OF PERCHLORIC ACID

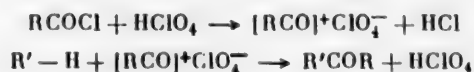
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p. 3145, September, 1961

Original article submitted March 2, 1961

Continuing our investigations in the field of catalytic acylation of organic compounds an anhydrides of carboxylic acids in the presence of perchloric acid [1], we found that the acyl chlorides of carboxylic acids, which are more readily obtainable, may be used as acylating agents. The reaction probably takes place according to the following mechanism, via stage of formation of acyl perchlorates, which are also acylating agents.



Acylation by acyl chlorides of carboxylic acids takes place readily when the components are boiled for a brief period in the presence of small catalytic amounts of perchloric acid. In this way we obtained 2,4,6-trimethylacetophenone (25%), p-methoxyacetophenone (17%), p-methoxybutyrophenone (54%), p-ethoxypropiofenone (36%), 2-acetothienone (52%) and other ketones.

The investigation is being continued.

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY
ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LEIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.-Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

NOTE: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. -Publisher.

Soviet Journals Available in Cover-to-Cover Translation

ABBREVIATION	RUSSIAN TITLE	TITLE OF TRANSLATION	PUBLISHER	TRANSLATION BEGAN
				Vol. Issue Year
AÉ	Atomnaya énergiya	Soviet Journal of Atomic Energy	Consultants Bureau	1 1 1956
Akust. zh.	Akusticheskiy zhurnal	Soviet Physics - Acoustics	American Institute of Physics	1 1 1955
Astr.(on). zh(um).	Antibiotiki	Antibiotics	Consultants Bureau	4 1 1959
Avto(mat). svarka	Astronomicheskii zhurnal	Soviet Astronomy-AJ	American Institute of Physics	34 1 1957
	Avtomaticheskaya svarka	Automatic Welding	British Welding Research Association (London)	
	Avtomatika i Telemekhanika	Automation and Remote Control	Instrument Society of America	1 1959
	Biofizika	Biophysics	National Institutes of Health*	27 1 1956
Byull. éksp(erim). biol. i med.	Biokhimiya	Biochemistry	Consultants Bureau	21 1 1957
DAN (SSSR)	Byulleten' éksp(erimental'noi biologii i meditsiny)	Bulletin of Experimental Biology and Medicine	Consultants Bureau	41 1 1959
Doklady AN SSSR	Doklady Akademii Nauk SSSR	The translation of this journal is published in sections, as follows:		
		Doklady Biochemistry Section	American Institute of Biological Sciences	106 1 1956
		Doklady Biological Sciences Sections (Includes: Anatomy, biophysics, cytology, ecology, embryology, genetics, histology, hydrobiology, microbiology, morphology, parasitology, endocrinology, evolutionary morphology, physiology, zoology sections)	American Institute of Biological Sciences	112 1 1957
		Doklady Botanical Sciences Sections (Includes: Botany, phytochemistry, plant anatomy, plant ecology, plant embryology, plant physiology, plant morphology sections)		
		Proceedings of the Academy of Sciences of the USSR, Section: Chemical Technology	Consultants Bureau	106 1 1956
		Proceedings of the Academy of Sciences of the USSR, Section: Chemistry	Consultants Bureau	106 1 1956
		Proceedings of the Academy of Sciences of the USSR, Section: Physical Chemistry	Consultants Bureau	112 1 1957
		Doklady Earth Sciences Sections (Includes: Geochemistry, geology, geophysics, hydrogeology, mineralogy, paleontology, petrography, permafrost sections)		
		Proceedings of the Academy of Sciences of the USSR, Section: Geochemistry	American Geological Institute	124 1 1959
		Proceedings of the Academy of Sciences of the USSR, Section: Geology	Consultants Bureau	106-1 1957-1959
		Proceedings of the Academy of Sciences of the USSR, Sections: Geology	Consultants Bureau	123 6 1956
		Doklady Soviet Mathematics	Consultants Bureau	106-1 1957-1959
		Soviet Physics-Doklady (Includes: Aerodynamics, astronomy, crystallography, cybernetics and control theory, electrical engineering, energetics, fluid mechanics, heat engineering, hydraulics, mathematical physics, mechanics, physics, technical physics, theory of elasticity sections)	The American Mathematics Society	123 6 1958
		Proceedings of the Academy of Sciences of the USSR, Applied Physics Sections (does not include mathematical physics or physics sections)		131 1 1961
		Wood Processing Industry		
		Telecommunications	American Institute of Physics	106 1 1956
		Entomological Review	Consultants Bureau	106-1 1956-1957
		Pharmacology and Toxicology	Timber Development Association (London)	9 1959
		Physics of Metals and Metallurgy	Massachusetts Institute of Technology*	1 1957
		Sechenov Physiological Journal USSR	American Institute of Biological Sciences	38 1 1959
		Plant Physiology	Consultants Bureau	20 1 1957
		Geochemistry	Acta Metallurgica*	5 1 1957
		Soviet Physics-Solid State	National Institutes of Health*	1 1957
		Measurement Techniques	American Institute of Biological Sciences	4 1 1957
		Bulletin of the Academy of Sciences of the USSR: Division of Chemical Sciences	The Geochemical Society	1 1958
			American Institute of Physics	1 1959
			Instrument Society of America	1 1959
			Consultants Bureau	1 1952
Derevoobrabat. prom-at.	Derevoobrabatvayushchaya promyshlennost'	Wood Processing Industry		
Éntom(ol). oboz(renie)	Élektrosvyaz	Telecommunications		
Farmakol. (i) toksikol(ogiya)	Éntomologicheskoe obozrenie	Entomological Review		
FMM	Farmakologiya i toksikologiya	Pharmacology and Toxicology		
Fiziol. zhurn. SSSR (im. Sechenova)	Fizika metallov i metallovedenie	Physics of Metals and Metallurgy		
Fiziol(ogiya) rast.	Fiziologicheskii zhurnal im. I. M. Sechenova	Sechenov Physiological Journal USSR		
FTT	Fiziologiya rastenii	Plant Physiology		
Izmerit. tekhn(ika)	Geokhimiya	Geochemistry		
Izv. AN SSSR, Otdel. Khim(um). N(auk)	Fizika tverdogo tela	Soviet Physics-Solid State		
	Izmeritel'naya tekhnika	Measurement Techniques		
	Otdelenie khimicheskikh nauk	Bulletin of the Academy of Sciences of the USSR: Division of Chemical Sciences		

continued

Izv. AN SSSR, Otd. (tekhn.) (Nauk): Met(All), i top.	(see Met. i top.)	Bulletin of the Academy of Sciences of the USSR: Physical Series	1	1954
Izv. AN SSSR Ser. fiz(ich).	Izvestiya Akademii Nauk SSSR: fizicheskaya	Bulletin (Izvestiya) of the Academy of Sciences USSR: Geophysics Series	1	1954
Izv. AN SSSR Ser. geofiz.	Izvestiya Akademii Nauk SSSR: Seriya geofizicheskaya	Izvestiya of the Academy of Sciences of the USSR: Geologic Series	1	1958
Izv. AN SSSR Ser. geol.	Izvestiya Akademii Nauk SSSR: Seriya geologicheskaya	Soviet Rubber Technology	18	1959
Kauch. i rez.	Kinetika i kataliz Koks i khimiya	Kinetics and Catalysis	1	1960
	Kolloidnyi zhurnal	Coke and Chemistry USSR	1	1958
Kolloidn. zh(urn).	Kristallografiya	Colloid Journal	1	1952
Metallov. i term. obrabot. metal.	Metallovedenie i termicheskaya obrabotka metallov	Metal Science and Heat Treatment of Metals	2	1957
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UFN	Uspekhi khimii	Russian Chemical Reviews	1	1960
UKh	Uspekhi matematicheskikh nauk	Russian Mathematical Surveys	1	1958
UMN	(see UFN)		1	1960
Usp. fiz. nauk	(see UMN)			
Usp. khim(ii)	Uspekhi sovremennoi biologii	Russian Review of Biology		
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Usp. sovr. biol.	Voprosy gematologii i perelivaniya krovi	Problems of Hematology and Blood Transfusion		
Vest. mashinostroyeniya	Voprosy onkologii	Problems of Oncology		
Vop. gem. i per. krovi	Voprosy virusologii	Problems of Virology		
Vop. onk.	Zavodskaya laboratoriya	Industrial Laboratory		
Vop. virusol	ZhNAKh Zh. anal(it). khimii	Journal of Analytical Chemistry USSR		
Zavodsk. lab(oratoriya)	ZhNETF			
ZhNAKh Zh. anal(it). khimii	Zh. eksperim. i teor. fiz.	Soviet Physics--JETP		
ZhNETF	ZhIFKh Zh. fiz. khimii	Russian Journal of Physical Chemistry		
Zh. eksperim. i teor. fiz.	ZhIMEI Zh(urn). mikrobiol. epidem(iol. i immunobiol.)	Journal of Microbiology, Epidemiology and Immunobiology		
ZhIFKh Zh. fiz. khimii	ZhNAKh Zh(urn). neorgan(ich). khim(ii)	The Russian Journal of Inorganic Chemistry		
ZhIMEI Zh(urn). mikrobiol. epidem(iol. i immunobiol.)	ZhNAKh Zh(urn). obshchei khimii	Journal of General Chemistry USSR		
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ZhOKh Zh(urn). obshchei khimii	ZhSKh Zh(urn). strukt. khimii	Journal of Structural Chemistry		
ZhPKh Zh(urn). prikl. khimii	ZhTF Zh(urn). tekhn. fiz.	Soviet Physics--Technical Physics		
ZhSKh Zh(urn). strukt. khimii	Zh(urn). vyssh. nervn. deyatel'nosti (im. I. P. Pavlova)	Pavlov Journal of Higher Nervous Activity		
ZhTF Zh(urn). tekhn. fiz.				
Zh(urn). vyssh. nervn. deyatel'nosti (im. I. P. Pavlova)				

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